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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

8-September-1999

Memorandum

Subject: PP#s 7F04910, 8F04997 - **Human Health Risk Assessment for the Food Use of Glufosinate Ammonium on Potatoes, Transgenic Sugar Beets and Transgenic Canola.** DP Barcodes: D257590, D258417. Submission #s: S545114, S529287. Case #s: 289177, 290273. Chemical #: 128850. EPA Registration Numbers: 45639-187 (Rely®) and 45639-199 (Liberty™).

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AgrEvo requests the establishment of a permanent registration for use of glufosinate ammonium on potatoes, transgenic sugar beets and transgenic canola. A summary of the human health risk resulting from the requested and registered uses of glufosinate ammonium is provided in this document. The hazard assessment was provided by Myron S. Ottley, Ph.D. of Registration Action Branch I (RAB1), the residue chemistry and dietary exposure assessment was provided by Tom Bloem of RAB1, the occupational and residential risk assessment was provided by Myrta Christian of RAB1, and the water exposure assessment was provided by Laurence Libelo of the Environmental Fate and Effects Division (EFED).

TABLE OF CONTENTS

1.0 EXECUTIVE SUMMARY

The petitioner is requesting registration of Liberty™ Herbicide (18.19% glufosinate ammonium; EPA Reg. No. 45639-199) for use on the transgenic varieties of sugar beet and canola and Rely® Herbicide (11.33% glufosinate ammonium; EPA Reg. No. 45639-187) for use in potato vine dessication. Concentrations of active ingredient in the formulated products are reported in terms of the racemic mixture (D and L isomers). Only the L isomer is herbicidally active.

Glufosinate ammonium is a non-selective, postemergent herbicide which acts as an inhibitor of glutamine synthetase, a critical enzyme in ammonium fixation and detoxification in plant cells. Formulated products of glufosinate ammonium are water soluble concentrates which are applied as a foliar spray. Current registrations include broadcast application to apple, grape, banana and tree nut orchards (time-limited tolerances ranging from 0.05 - 0.3 ppm) and to the transgenic varieties of field corn and soybeans (time-limited tolerances ranging from 0.2 - 25.0 ppm). Tolerances are also established as a result of secondary residues in milk, eggs, and the meat, fat and meat byproducts of ruminants and poultry (time-limited tolerances ranging from 0.05 ppm - 0.10 ppm). Prior to this petition, tolerances were established on a time-limited basis due to a lack of a rat carcinogenicity study. A Section 18 request from Wisconsin for use on transgenic sweet corn has been approved (4.0 ppm tolerance).

Hazard Profile

Glufosinate ammonium (racemic mixture of glufosinate ammonium; D and L isomer) is in toxicity category III for acute oral, dermal and inhalation toxicities and for eye irritation. It is not a dermal irritant or sensitizer. For subchronic toxicity, the primary effects of concern in the mouse were increased liver and kidney weights with increases in serum aspartate amino transferase and alkaline phosphatase. Signs of neurotoxicity, such as aggressive behavior, piloerection, high startle response, and increased incidence of fearfulness, were observed in subchronic rat studies.

Chronic studies in the rat demonstrated increased mortality, increased occurrence of retinal atrophy, inhibition of brain glutamine synthetase, and increased liver and kidney weights. In the mouse, increase mortality and changes in glucose levels consistent with changes in glutathione levels were observed. Increased mortality and EKG alterations were observed in dogs. There was no evidence of a treatment-related increase in tumors in rats and mice.

The developmental toxicity study in the rat resulted in dilated renal pelvis and/or hydroureter in the offspring at levels that resulted in significant increases in hyperactivity and vaginal bleeding in dams. In the rabbit, decreased fetal body weight and increased fetal mortality were observed; while in rabbit does, decreased food consumption, body weight and body weight gain were observed. The reproductive toxicity study indicated systemic and postnatal developmental toxicity in the form of increased kidney weights in parents and a decrease in viable pups in all generations.

Based on the lack of mutagenic potential as assessed in a battery of mutagenic assays, and the absence of treatment-related tumors in rats and mice at dose levels adequate for assessment, glufosinate ammonium has been classified as a "not likely" human carcinogen.

A dermal absorption study with rats indicated that about 50% of the given radioactivity was absorbed 48 hours after a single dose application. In other metabolism studies, it was shown that over 80% of administered radioactivity is excreted within 24 to 48 hours as the parent compound in the feces and urine. Highest tissue levels were found in liver, kidney and gonads.

Additional testing was conducted using 3-methylphosphinico propionic acid, N-acetyl glufosinate and the L-isomer of glufosinate ammonium (major metabolites found in plants and animals). These compounds, tested in subchronic rat, mouse and dog studies, and in developmental toxicity studies in rat and rabbit, showed a similar toxicity profile as the racemic mixture of glufosinate ammonium (D- and L-isomers). Since formulated products of glufosinate ammonium are a racemic mixture of the D and L isomers, HOE 039866 (DL-glufosinate ammonium) is the compound that is deemed appropriate for endpoint selection.

FQPA Safety Factor

There are no guideline data gaps for assessment of glufosinate ammonium following *in utero* and/or postnatal exposure. The data provided no indication of increased susceptibility in rats or rabbits to pre or postnatal exposure to glufosinate ammonium. A consistent pattern of neurotoxicity was seen in several studies, including the subchronic, developmental, and chronic studies in rats, mice and dogs. In addition to the clinical signs, such as hyperactivity, aggressive behavior, piloerection, and high startle response, retinal atrophy was observed. Changes in glutamine synthetase levels were observed in liver, kidney and brain in rats. Based on the toxicity profile, HED is requesting acute, subchronic and developmental neurotoxicity studies in rats. **Although there were no signs of increased susceptibility, the FQPA Safety Factor Committee determined that a safety factor of 3 should be retained because of data gaps for the assessment of neurotoxicity. The FQPA safety factor is applicable to all population subgroups and risk assessments (acute/chronic dietary and residential).**

Toxicological Endpoints

Acute Dietary: An acute RfD was not established for the general population. No appropriate toxicological endpoint attributable to a single exposure was identified in the available toxicity studies. However, an acute RfD of 0.063 mg/kg/day was established for the females 13 - 50 subgroup, based on a developmental NOAEL of 6.3 mg/kg/day in the rabbit and a 100x uncertainty factor (10x inter- 10x intra-species extrapolation). The developmental LOAEL (20 mg/kg/day) was based on reduced fetal body weight and increased fetal death. Using a 3x FQPA safety factor, the acute population adjusted dose (aPAD) for glufosinate ammonium is 0.021 mg/kg/day.

Chronic Dietary (non-cancer): The chronic RfD of 0.021 mg/kg/day was established, based on the NOAEL of 2.1 mg/kg/day in the 2-year chronic study in rats and a 100x uncertainty factor (10x inter- 10x intra-species extrapolation). The LOAEL in this study was based on increased kidney weight and kidney/brain weight in males at 52 weeks (6.8 mg/kg/day) and decreased survival in females at 130 weeks (8.2 mg/kg/day). Using a 3x FQPA safety factor, the cPAD for glufosinate ammonium is 0.007 mg/kg/day.

Short-, Intermediate- and Long-Term Dermal: The FQPA safety factor of 3 is applicable to residential risk assessments only (acceptable MOE of 300 for residential and 100 for occupational risk assessments).

Short- and intermediate-term dermal risk assessments were recommended based on neurological clinical signs (hyperactivity, aggressive behavior, piloerection) observed in the 21-day dermal study in rats at 300 mg/kg/day (LOAEL). The NOAEL was 100 mg/kg/day.

Long-term dermal risk assessment was recommended based on the NOAEL of 2.1 mg/kg/day established in the 2-year chronic study in rats (see chronic dietary; 50% dermal absorption).

Short- and Intermediate-Term Inhalation: With the exception of an acute inhalation study, no inhalation studies are available. Therefore, oral NOAELs were selected for inhalation risk assessments. Since an oral dose is used, the exposure assessments will be conducted by converting the application rate to oral equivalents and assuming 100% absorption. The FQPA safety factor of 3 is applicable to residential risk assessments only (acceptable MOE of 300 for residential and 100 for occupational risk assessments).

Short-term inhalation risk assessments were recommended based on the developmental NOAEL of 6.3 mg/kg/day in the rabbit (see acute dietary endpoint).

Intermediate-term inhalation risk assessments were recommended based on the NOAEL of 2.1 mg/kg/day from the 2-yr chronic rat study (see chronic dietary endpoint).

Drinking Water Exposure Assessment

Glufosinate ammonium is water soluble and stable to hydrolysis and photolysis. The soil and aquatic anaerobic half-lives of glufosinate ammonium are such that sustained concentration in surface water is not likely. Due to the high water solubility of glufosinate ammonium, it will reach ground water relatively quickly and thereby counteract the degradation seen in surface water. The Environmental Fate and Effects Division (EFED) estimates acute and chronic ground water concentrations at 1.16 ppb (SCI-GROW) and acute and chronic surface water concentrations at 34.1 ppb and 0.79 ppb, respectively (PRZM/EXAMS; Tier 2).

Occupational/Residential Risk Estimates

Occupational: The proposed use on potatoes and the transgenic varieties of canola and sugar beets will result in short- and intermediate-term exposures to mixer/loaders and applicators. Post-application occupational exposure is not anticipated to be a concern based on the use pattern and the fact that planting and harvesting of the subject crops are mechanized. The potential short- and intermediate-term exposures to workers (commercial and private) do not exceed HED's level of concern (estimated MOEs > 350).

Residential: Glufosinate ammonium is registered for residential use as a spot treatment around trees, shrubs, fences, walks, patios, driveways, sidewalks, and flower beds. It is also registered for lawn renovation uses. Only short-term residential exposures are expected from the registered uses of glufosinate ammonium. The contribution from inhalation exposures to the overall risk was not significant. **The handler and post-application dermal exposure estimates from the existing residential uses are above HED's level of concern (handler MOE of 217 [garden use]; post-application MOEs of 100 for adults and 110 for children [lawn renovation use]).** Due to the lack of chemical specific data, the dermal exposure estimates were based on high-end scenarios and assumptions for regular lawn uses (from the Draft HED SOPs for residential exposure assessment), which are not necessarily applicable to lawn renovation uses. These assumptions represent a Tier 1 assessment and therefore are expected to overestimate the real potential risk.

Aggregate Risk Estimates

Acute Aggregate Risk: The acute dietary exposure analysis for females 13 - 50 (no acute dietary endpoint was identified for the general US population including infants and children) assumed tolerance level residues and 100% crop treated for all registered and proposed commodities (Tier 1 analysis). The most highly exposed population among females 13 - 50 was nursing females at 58% of the aPAD (95th percentile). The estimated glufosinate ammonium concentrations in surface (34.1 ppb) and ground water (1.16 ppb) are less than HED's drinking water level of comparison (DWLOC; 270 ppb for females 13 - 50 nursing). Acute aggregate exposure to glufosinate ammonium, as a result of all registered and proposed uses, is below HED's level of concern.

Chronic Aggregate Risk: Since there are no chronic residential exposure scenarios, the chronic aggregate risk assessment is concerned with food and water only. The chronic dietary exposure analysis assumed tolerance level residues for all registered and proposed commodities and incorporated the weighted average percent crop treated for all registered commodities (sweet corn maintained at 100% crop treated; Tier 2 analysis). For the most highly exposed subgroup (children, 1-6 years), 71% of the cPAD is occupied by dietary (food) exposure. The estimated glufosinate ammonium concentrations in surface (0.79 ppb) and ground water (1.16 ppb) are less than HED's DWLOC (20 ppb for children 1-6 years). Chronic aggregate exposure to glufosinate ammonium, as a result of all registered and proposed uses, is below HED's level of concern.

Aggregate Short- and Intermediate-Term Risk: Short- and intermediate-term aggregate risk assessments include average dietary exposure (food and water) and short- or intermediate-term dermal and inhalation exposures from residential uses. The dermal exposure estimates from the registered residential uses of glufosinate ammonium are above HED's level of concern (inhalation exposures were insignificant). According to HED policy (HED SOP 97.2), the residential dermal exposures cannot be aggregated with chronic dietary exposure because different endpoints were chosen for these exposure scenarios.

Recommendations for Tolerances

The potential risks (from dermal exposures) for the registered residential lawn renovation use are above HED's level of concern. However, these risks result from toxic effects that are different from the ones attributed to dietary exposure. Therefore, the estimated risks from the residential uses cannot be aggregated to the potential dietary risk. The HED Risk Assessment Review Committee concluded the following (RARC Report, 24-Aug-1999):

> This risk assessment is unique in that the dermal and dietary endpoints are completely different. A reasonable argument could be made for this particular food use safety finding: Dietary risk plus all other risks with the same toxic effect do not result in an aggregate risk concern; since this petition deals only with dietary risks and water (both using oral endpoints), there is no unacceptable risk considering the only toxicity endpoint associated with this petition. Toxicity expected from the dermal exposure route does not contribute to the risk considering only the oral endpoints which are the only ones associated with the proposed uses. The RARC recommended that RD and OGC be consulted to determine the best course.

The following deficiencies were identified in the toxicological and residue chemistry databases:

- Acute Neurotoxicity, Subchronic Neurotoxicity and Developmental Neurotoxicity Studies (Guidelines 81-8, 82-7 and 83-3; respectively)
- A Revised Section B (Liberty™ and Rely®)
- Storage stability Study for Sugar Beet Processed Commodities (sugar, pulp and molasses; 3 months; Guideline 860.1380)
- Successful Petition Method Validation for Methods BK/04/95 (sugar beets) and HRAV-24 (canola)

Pending resolution of the deficiencies listed above and the residential exposure issues, HED concludes that the toxicological, residue chemistry and occupational exposure databases support the establishment of the following tolerances, for the combined residues of glufosinate ammonium, N-acetyl glufosinate and 3-methylphosphinico propionic acid, expressed as glufosinate free acid equivalents.

Beet, Sugar, tops (Leaves)	1.5 ppm
Beet, Sugar, root	0.9 ppm
Beet, Sugar, molasses	5.0 ppm
Canola, seed	0.4 ppm
Canola, meal	1.1 ppm
*Potato	0.8 ppm
*Potato, chips	1.6 ppm
*Potato, granules/flakes	2.0 ppm

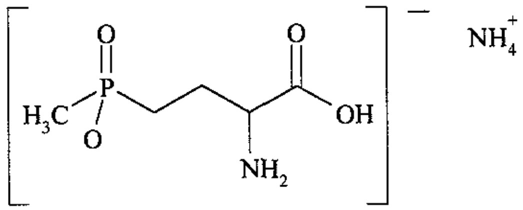
* Tolerance expression for commodities derived from potatoes are for the combined residues of glufosinate ammonium and 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents (non-transgenic crop).

Since glufosinate ammonium has been classified as a "not likely" human carcinogen, the previously established time-limited tolerances can be made permanent.

2.0 PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION

Glufosinate-ammonium (herbicide) is a racemic mixture of the D and L isomers; only the L-isomer is herbicidally active. Concentrations in the technical and formulated products are reported in terms of the racemic mixture. Impurities present in the technical grade product and in the end use product are not presently considered to be of toxicological concern.

Chemical Name:	ammonium-DL-homoalanin-4-yl (methyl phosphinate)
Common Name:	glufosinate ammonium
PC Code Number:	128850
CAS Registry No.:	77182-82-2
Empirical Formula:	$C_5H_{15}N_2O_4P$
Molecular Weight:	198.19
Vapor Pressure:	not determinable
Partition Coefficient (n-Octanol/Water):	<0.1
Water Solubility:	1370 mg/l



3.0 HAZARD CHARACTERIZATION

The HIARC (Memo, M.S. Ottley, 17-May-1999) and FQPA Safety Factor Committee (Memo, B. Tarplee, 17-May-1999) reports are included as Attachments 1 and 2, respectively.

3.1 Hazard Profile (Tables 1 and 2)

Glufosinate ammonium (also referred to as DL-glufosinate ammonium or HOE 039866) is toxicity category III for acute oral, dermal, and inhalation toxicities, and for eye irritation. It is not a dermal irritant or sensitizer. For subchronic toxicity, the primary effects in the mouse were increased liver and kidney weights with increases in serum aspartate amino transferase and alkaline phosphatase. Signs of neurotoxicity were observed in rats in subchronic studies, such as aggressive behavior, piloerection, high startle response, and increased incidence of fearfulness.

In the chronic rat studies, increased mortality, increased occurrence of retinal atrophy, and inhibition of brain glutamine synthetase were observed, as were increased liver and kidney weights. In the mouse, increased mortality was observed, as were changes in glucose levels consistent with changes in glutathione levels. Increased mortality and EKG alterations were observed in dogs. **There was no evidence of a treatment-related increase in tumors in rats and mice.**

The developmental toxicity study in the rat resulted in dilated renal pelvis and/or hydroureter in the offspring at levels that resulted in significant increases in hyperactivity and vaginal bleeding in dams. In the rabbit, decreased fetal body weight and increased fetal mortality were observed at 20 mg/kg/day; while in rabbit does, decreased food consumption, body weight, and body weight gain were observed at 6.3 mg/kg/day.

The reproductive toxicity study indicated systemic and postnatal developmental toxicity at 6.0 mg/kg/day in the form of increased kidney weights in parents, and a decrease in viable pups in all generations. Since parental and developmental effects were observed at the same dose levels, **there is no evidence of increased susceptibility in offspring.**

A **consistent pattern of neurotoxicity was seen** in several studies, including the subchronic, developmental and chronic studies in rats, mice and dogs. In addition to the clinical signs, such as hyperactivity, aggressive behavior, piloerection, and high startle response, retinal atrophy was observed. Changes in glutamine synthetase levels were observed in liver, kidney and brain in rats. Based on the toxicity profile, HED is requesting acute, subchronic and developmental neurotoxicity studies in rats (HIARC Report, 17-May-1999). It is expected that these studies will provide the information needed to further characterize the neurotoxic effects.

There is no concern for mutagenic activity as indicated in the following studies: Salmonella E. Coli, *in vitro* mammalian cell gene mutation assays, mammalian cell chromosome aberration assays, *in vivo* mouse bone marrow micronucleus assays, and unscheduled DNA synthesis assays.

A dermal absorption study in rats indicated that about 50% of the given radioactivity was absorbed 48 hours after a single dose application. In other metabolism studies, it was shown that over 80% of administered radioactivity is excreted within 24 to 48 hours as the parent compound in the feces and urine. Highest tissue levels were found in liver, kidney and gonads.

Additional testing was conducted with the following major metabolites: HOE 061517 (3-methylphosphinico propionic acid, HOE 099730 (N-acetyl glufosinate), as well as HOE 058192 (L-isomer of the parent). These compounds, tested in subchronic rat, mouse and dog studies, and in developmental toxicity studies in rat and rabbit, showed a similar profile of toxicity as the parent compound (HOE 039866). Since formulated products of glufosinate ammonium are a racemic mixture of the D and L isomers, HOE 039866 (DL-glufosinate ammonium) is the compound that is deemed appropriate for endpoint selection.

Data Gaps: Three data gaps have been identified at this time: acute neurotoxicity, subchronic neurotoxicity and developmental neurotoxicity. These studies are requested because of concern for the neurotoxic effects observed in several studies and in multiple species. It is also requested that glutamine synthetase levels be measured in the subchronic neurotoxicity study to assist the Agency in characterizing these effects.

Table 1: Acute Toxicity of Glufosinate Ammonium Technical

Study Type	Results	Toxicity Category
81-1 acute oral–rat MRID 41796102	LD_{50} 4010 mg/kg in males LD_{50} 3030 mg/kg in females	III
81-2 acute dermal MRID 41796103	LD_{50} > 2000 mg/kg in males & females	III
81-3 acute inhalation MRID 41846302	LC_{50} 4.42 mg/L estimated in males & females	III
81-4 eye irritation MRID 072962	eye irritant; corneal opacity reversible within 7 days	III
81-5 dermal irritation MRID 41796105	not a dermal irritant	IV
81-6 sensitization MRID 41796106	not a dermal sensitizer	NA

Table 2: Subchronic and Chronic Toxicity Profile of Glufosinate Ammonium [1]

[1]Study Type	MRID	NOAEL (mg/kg/day)	LOAEL (mg/kg/day)	Based On
2-YR FEED/CARCINOGENIC RAT (HOE 039866) (1986)	40345607	2.1 mg/kg/day	6.8 / 8.2 mg/kg/day (M/F) No evidence of ⇑ tumors	⇑ kidney & brain wt in males, ⇑ mortality in females NO TUMORS Inhibition (11%) brain GS Females at 28.7 mg/kg
18-MN CARCINOGENIC MOUSE (HOE 039866) (1986)	41144702	10.82 / 16.19 mg/kg/day (M/F)	22.60 / 63.96 mg/kg/day (M/F) No evidence of ⇑ tumors	⇑mortality & glucose levels, consistent changes in glutathione levels, etc.
2-YR CARCINOGENICITY RAT (HOE 039866) (1989)	44539501	45.4 / 57.1 mg/kg/day (M/F)	228.9 / 281.5 mg/kg/day (M/F) No evidence of ⇑ tumors	⇑ levels of retinal atrophy.
1-YR CHRONIC FEEDING DOG (HOE 039866) (1989)	40345608	5.0 mg/kg/day	8.5 mg/kg/day	⇑ mortality alterations in EKG
2-GEN. REPRO. RAT (HOE 039866) (1988)	40345612	systemic: 2 mg/kg/day repro/develop: 6 mg/kg/day	systemic 6 mg/kg/day repro/develop: 18 mg/kg/day	⇑kidney wts M + F decr viable pups in all generations
DEVELOP. TOXICITY RAT (HOE 039866) (1986)	40345610	maternal: 10 mg/kg/day develop: 250 mg/kg/d	maternal: 50 mg/kg/day develop.: 250 mg/kg/day	vaginal bleeding and hyperactivity dilated renal pelvis and/or hydroureter
DEVELOP. TOXICITY RABBIT (HOE 039866) (1984)	4114703	maternal: 2.0 mg/kg/day develop: 6.3 mg/kg/day results shown in table 3 of DER. NOT CLEAR-CUT	maternal: 6.3 mg/kg/day develop: 20 mg/kg/day	⇓food consumption ⇓ BW & BW gain, ⇑ kidney wt absent/incomplete ossification ⇓ body weights fetal death
13-WEEK FEEDING MOUSE (HOE 039866) (1986)	40345609	48 mg/kg/day (M) 192 mg/kg/day (F)	192 mg/kg/day (M) >192 mg/kg/day (F)	⇑ rel & abs kidney & liver weights. ⇑ (30% M) serum aspartate amino transferase ⇑ (38% females) serum alkaline phosphatase
21-DAY DERMAL RAT (HOE 039866) (1985)	40345605	100 mg/kg/day	300 mg/kg/day	aggressive behavior, piloerection, high startle response
METABOLISM RAT (HOE 039866) 1993	43766913			Excreted in 24 hr, mostly as parent cpd. 80% M 73% F.

[1]Study Type	MRID	NOAEL (mg/kg/day)	LOAEL (mg/kg/day)	Based On
METABOLISM RAT (HOE 039866) (1995)	43766914 43778402			excr in 24- 48 hr. as parent cpd 80% M 88% F little sequestered in tissues.
METABOLISM Single Oral Dose in Rat (HOE 039866) (1985)	40345640			excreted as parent 88/84% in M/F, resp. highest levels in liver kidney gonads
METABOLISM Repeated Oral Dose in Rat (HOE 039866) (1985)	40345642			major route is feces. Increased radioactivity in tissue compared with single dose study.
13-WK FEEDING MOUSE (HOE 061517 metabolite) (1989)	44076207	1121 / 1340 mg/kg/day (M/F)	not established	not applicable
13-WK FEEDING RAT (HOE 061517 metabolite) (1989)	44076206	102 mg/kg/day	420 mg/kg/day	Males only: marginal liver wt incr. & ↑ incid. of small Kupffer cell proliferates and ↑ reticulocyte counts.
13-WEEK FEEDING DOG (HOE 099730 metabolite) (1994)	44076201	147 / 162 mg/kg/day (M/F)	738 / 800 mg/kg/day (M/F)	inhibition of brain glutamine synthetase
14-WK ORAL FEEDING RAT (HOE 058192 isomer) (1989)	44068501	18.5 / 19.8 mg/kg/day (M/F)	91.8 / 100.3 mg/kg/day (M/F)	↑ NH_3 levels in plasma & urine, slight ↑ kidney wt
13-WEEK FEEDING DOG (HOE 099730 metabolite) (1989)	44076203	19 / 21 mg/kg/day (M/F)	72 / 79 mg/kg/day (M/F)	inhibition of brain glutamine synthetase
13-WEEK FEEDING DOG (HOE 058192 isomer) (1989)	44068502	2 mg/kg/day	5 mg/kg/day	↑ NH_3 levels in plasma & kidney.
DEVELOP. TOXICITY RAT (HOE 099730 metabolite) (1992)	44076204	Maternal: 1000 mg/kg/day Develop: 1000 mg/kg/day	Maternal: > 1000 mg/kg/day Develop: > 1000 mg/kg/day	not applicable
DEVELOP. TOXICITY RAT (HOE 061517 metabolite) (1994)	44076209	maternal: 300 mg/kg/day develop: 300 mg/kg/day	maternal: 900 mg/kg/day develop.: 900 mg/kg/day	one death, persistent piloerection and/or ↑ urinary output, ↑abs kidney wt. ↑ incidence of total litter loss ↑ incidence (fetal & litter) of wavy and/or thickened ribs.

[1]Study Type	MRID	NOAEL (mg/kg/day)	LOAEL (mg/kg/day)	Based On
DEVELOP. TOXICITY RABBIT (HOE 058192 isomer) (1992)	43829405	maternal: 1.25 mg/kg/day develop: 1.25 mg/kg/day	maternal: 2.5 mg/kg/day develop: 2.5 mg/kg/day	↓bw & bw gain & food consumption; neurotoxic signs (severe spasms, lateral recumbency, muscle twitching), abortions ↑ fetal resorptions
DEVELOP. TOXICITY RABBIT (HOE 099730 metabolite) (1995)	44076205	maternal: 64 mg/kg/day develop: 64 mg/kg/day	maternal: 160 mg/kg/day develop: 160 mg/kg/day	reduced food consumption uni or bilateral extra rib at the 13th thoracic vertebra
DEVELOP. TOXICITY RABBIT (HOE 061517 metabolite) (1994)	44076210	maternal: 50 mg/kg/day develop: 200 mg/kg/day	maternal: 100 mg/kg/day develop: >200 mg/kg/day	↓ food & water consumption, fecal output; ↑abortions and mortality no develop effects.
PHARMACOKINETICS WITH DERMAL APPLICATION (HOE 039866) (1986)	40345620			42.5 to 50% absorbed at 0.1 mg 26% absorbed at 10 mg. Mostly excreted via urine. Minimal amounts in brain relative to liver and kidney
13-WK FEEDING MOUSE (HOE 99730 metabolite) (1994)	44076202	<83 mg/kg/day (M) 110 mg/kg/day (F)	83 mg/kg/day (M) 436 mg/kg/day (F)	inhibition of brain glutamine synthetase
MUTAGENICITY: DNA Damage & Repair (HOE 039866) (1984) Gene Mutation (HOE 039866) (1984)	072962 072962	not mutagenic not mutagenic		no DNA damage no reverse mutation
MUTAGENICITY: Unscheduled DNA Synthesis (HOE 039866) (1984)	40345614	not mutagenic		no evidence of inhibition of DNA synthesis
MUTAGENICITY: Mouse Lymphoma Forward Mutation (HOE 039866) (1988)	40345616	not mutagenic		did not increase mutation frequency
MUTAGENICITY: Mouse micronucleus assay (HOE 039866) (1986)	41144704	non-mutagenic		no effect on micronucleus formation

[1] HOE 039866 = glufosinate ammonium, HOE 058192 = L-isomer of glufosinate ammonium, HOE 061517 = 3-methylphosphinico propionic acid, HOE 099730 = N-acetyl glufosinate

3.2 FQPA Considerations

There are no guideline data gaps for assessment of glufosinate ammonium following *in utero* and/or postnatal exposure. The data provide no indication, either quantitatively or qualitatively, of increased susceptibility in rats or rabbits, to pre- and/or post-natal exposure to glufosinate ammonium. In the prenatal developmental toxicity studies in rats and rabbits and the two-generation reproductive study in rats, any observed toxicity to the fetuses or offspring occurred at equivalent or higher doses as the toxicity to parental animals. A consistent pattern of neurotoxicity was seen in several studies, including the subchronic, developmental and chronic studies in rats, mice and dogs. In addition to the clinical signs such as hyperactivity, aggressive behavior, piloerection, and high startle response, retinal atrophy was observed. Changes in glutamine synthetase levels were observed in liver, kidney and brain in rats. Based on the toxicity profile, acute, subchronic and developmental neurotoxicity studies in rats were requested (HIARC Report, 17-May-1999). **Although there were no signs of increased susceptibility, the FQPA Safety Factor Committee determined that a safety factor of 3 should be retained because of data gaps for the assessment of neurotoxicity. The FQPA safety factor is applicable to all population subgroups and risk assessments (acute/chronic dietary and residential).**

3.3 Dose Response Assessment

Acute Dietary: An acute RfD was not established for the general population. No appropriate toxicological endpoint attributable to a single exposure was identified in the available toxicity studies. However, an acute RfD of 0.063 mg/kg/day was established for the females 13 - 50 subgroup, based on a developmental NOAEL of 6.3 mg/kg/day in the rabbit and a 100x uncertainty factor (10x inter- 10x intra-species extrapolation). The developmental LOAEL (20 mg/kg/day) was based on reduced fetal body weight and increased fetal death. Using a 3x FQPA safety factor, the aPAD for glufosinate ammonium is 0.021 mg/kg/day.

Chronic Dietary (non-cancer): The chronic RfD of 0.021 mg/kg/day was established, based on the NOAEL of 2.1 mg/kg/day in the 2-year chronic study in rats and a 100x uncertainty factor (10x inter- 10x intra-species extrapolation). The LOAEL in this study was based on increased kidney weight and kidney/brain weight in males at 52 weeks (6.8 mg/kg/day) and decreased survival in females at 130 weeks (8.2 mg/kg/day). Using a 3x FQPA safety factor, the cPAD for glufosinate ammonium is 0.007 mg/kg/day.

Chronic Dietary (cancer): Glufosinate ammonium has been classified as a **"not likely"** human carcinogen according to the EPA *Proposed Guidelines for Carcinogen Risk Assessment*. The HED HIARC assigned this classification to glufosinate ammonium (HED Doc. No 013385) based on the lack of mutagenic potential as assessed in a battery of mutagenicity assays, and the absence of treatment-related tumors in rats and mice at dose levels adequate for assessment.

Short-, Intermediate- and Long-Term Dermal: The FQPA safety factor of 3 is applicable to residential risk assessments only (MOE of 300 for residential and 100 for occupational risk assessments).

Short- and intermediate-term dermal risk assessments were recommended based on neurological clinical signs (hyperactivity, aggressive behavior, piloerection) observed in the 21-day dermal study in rats at 300 mg/kg/day (LOAEL). The NOAEL was 100 mg/kg/day.

Long-term dermal risk assessment was recommended using the oral NOAEL of 2.1 mg/kg/day established in the 2-year chronic study in rats (see chronic dietary; 50% dermal absorption).

Short- and Intermediate-Term Inhalation: With the exception of an acute inhalation study, no inhalation studies are available. Therefore, oral NOAELs were selected for inhalation risk assessments. Since an oral dose is used, the exposure assessments will be conducted by converting the application rate to oral equivalents and assuming 100% absorption. The FQPA safety factor of 3 is applicable to residential risk assessments only (MOE of 300 for residential and 100 for occupational risk assessments).

Short-term inhalation risk assessments were recommended using the developmental NOAEL of 6.3 mg/kg/day in the rabbit (see acute dietary endpoint).

Intermediate-term inhalation risk assessments were recommended using the oral NOAEL of 2.1 mg/kg/day from the 2-yr chronic rat study (see chronic dietary endpoint).

Table 3: Endpoint Selection Summary

Exposure Scenario	Dose (mg/kg/day)	Endpoint	Study
Acute Dietary	developmental NOAEL = 6.3 [1]UF = 300	LOAEL = 20 mg/kg/day based on decreased fetal body weight and increased fetal death	developmental toxicity–rabbit
		Acute RfD = 0.063 mg/kg/day (females 13 - 50only) **aPAD** = 0.021 mg/kg/day no acute RfD for the general population including infants and children was identified	
Chronic Dietary	NOAEL = 2.1 [1]UF = 300	LOAEL = 6.8 / 8.2 mg/kg/day in males / females based on increased kidney weight and kidney/brain weight in males at 52 weeks, and decreased survival in females at 130 weeks.	Two-year chronic toxicity/carcinogenicity in rat
		Chronic RfD = 0.021 mg/kg/day **cPAD** = 0.007 mg/kg/day	
Short-Term (Dermal)	NOAEL = 100 [2]MOE = 300	LOAEL = 300 mg/kg/day based on clinical observations (aggressive behavior, piloerection & high startle response)	21-day dermal-rat
Intermediate-Term (Dermal)	NOAEL = 100 [2]MOE = 300	LOAEL = 300 mg/kg/day based on clinical observations (aggressive behavior, piloerection & high startle response)	21-day dermal-rat
Long-Term (Dermal)	NOAEL = 2.1 [2]MOE = 300	LOAEL = 6.8 / 8.2 mg/kg/day **oral** in males / females based on increased kidney weight and kidney/brain weight in males at 52 weeks, and decreased survival in females at 130 weeks. **50% dermal absorption demonstrated.**	Two-year chronic oral toxicity/carcinogenicity in rat
Short-Term (Inhalation)	developmental NOAEL = 6.3 [2]MOE = 300	LOAEL = 20 mg/kg/day based on decreased fetal body weight and increased fetal death	developmental toxicity–rabbit

Exposure Scenario	Dose (mg/kg/day)	Endpoint	Study
Intermediate-Term (Inhalation)	NOAEL = 2.1 [2]MOE = 300	LOAEL = 6.8 / 8.2 mg/kg/day **oral** in males / females based on increased kidney weight and kidney/brain weight in males at 52 weeks, and decreased survival in females at 130 weeks.	Two-year chronic oral toxicity/carcinogenicity in rat
Long-Term (Inhalation)	NOAEL = 2.1 [2]MOE = 300	LOAEL = 6.8 / 8.2 mg/kg/day **oral** in males / females based on increased kidney weight and kidney/brain weight in males at 52 weeks, and decreased survival in females at 130 weeks.	Two-year chronic oral toxicity/carcinogenicity in rat

1 UF = uncertainty factor; 100 for intra/inter species extrapolation and 3 for FQPA safety factor
2 acceptable MOEs; 300 for residential risk assessments and 100 for occupational risk assessments (FQPA safety factor not applied to occupational risk assessments)

4.0. EXPOSURE ASSESSMENT

A complete review of information pertaining to residue chemistry can be found in Attachment 3 (D257629 & D257628, T. Bloem, 9-July-1999).

4.1 Summary of Registered/Requested Uses

Glufosinate ammonium is a non-selective, postemergent herbicide which acts as an inhibitor of glutamine synthetase, a critical enzyme in ammonium fixation and detoxification in plant cells. Formulated products of glufosinate ammonium are water soluble and applied as a foliar spray. Current registrations include use on both transgenic and non-transgenic crops. Transgenic plants contain a gene (phosphiothrion-acetyl-transferase) which enables the plant to metabolize the herbicidally active moiety of glufosinate-ammonium into a N-acetyl glufosinate (2-acetamido-4-methylphosphinico-butanoic acid; not herbicidally active). This metabolite is found only in transgenic plants. The tolerance expression for non-transgenic crops and animal commodities includes glufosinate ammonium and 3-methylphosphinico propionic acid. The tolerance expression for transgenic crops includes these two compounds along with the N-acetyl glufosinate metabolite.

Current registrations include broadcast application to apple, grape, banana and tree nut orchards (4.5 lbs ai/acre/year; pre-harvest interval (PHI) = 14 days; time-limited tolerances ranging from 0.05 - 0.3 ppm) and to the transgenic varieties of field corn and soybeans (0.73 lb ai/acre/season; PHI = 60 days for corn forage and 70 days for corn grain, corn fodder, and soybean seed; time-limited tolerances ranging from 0.2 - 25.0 ppm). Tolerances are also established as a result of secondary residues in milk, eggs, and the meat, fat and meat byproducts of ruminants and poultry (time-limited tolerances ranging from 0.05 ppm - 0.10 ppm). Prior to this petition, tolerances were established on a time-limited basis due to a lack of a rat carcinogenicity study. A Section 18 request from Wisconsin for use on transgenic sweet corn has been approved (0.64 lb ai/acre/season; PHI = 70 days; 4.0 ppm tolerance). Residential registrations include use in lawn renovation and spot treatment.

The petitioner is requesting registration of Liberty™ Herbicide (18.19% glufosinate ammonium; 1.67 lbs ai/US gallon; EPA Reg. No. 45639-199) for use on the transgenic varieties of sugar beet and canola and Rely® Herbicide (11.33% glufosinate ammonium; 1.00 lb ai/US gallon; EPA Reg. No. 45639-187) for use in potato vine dessication.

Sugar Beets: Applications of Liberty™ Herbicide may be made from the cotyledon stage up to the 10-leaf stage. The maximum recommended single application rate is 0.55 lb glufosinate ammonium/acre. A maximum of 1.1 lbs ai/acre can be applied per season. Applications can be made with ground or aerial equipment. The label specifies a 60-day pre-harvest interval (PHI).

Canola: Applications of Liberty™ Herbicide may be made from the cotyledon stage up to the early bolting stage (at this stage the plant has at least 6 leaves). A maximum of two applications per season is allowed with the total seasonal rate not to exceed 0.89 lb ai/acre. Applications can be made with ground or aerial equipment. The label specifies a 65-day PHI. The petitioner requested a higher use rate (1.56 lbs ai/acre/season) for canola grown for seed (seed retained for planting in the future).

Potato: Application of Rely® Herbicide is recommended at the beginning of natural vine senescence. The product is to be applied at a rate of 0.38 lb ai/acre with ground or aerial equipment. The label specifies a 9-day PHI. Potatoes grown for seed stock are not to be treated.

The Chemistry Science Advisory Committee determined that canola grown for seed is a food use and therefore requires a tolerance (Chem SAC Minutes, 21-Jul-1999). To establish a tolerance, the petitioner must submit field trial data reflective of the requested use rate (1.56 lbs ai/acre). Currently, HED has canola field trial data which demonstrates residue levels resulting form application of glufosinate ammonium at 0.71 - 0.98 lb ai/acre. Therefore, the information pertaining to the higher use rate for canola grown for seed should be eliminated from the Liberty™ label. The "Restrictions to the Directions for Use" section of the Liberty™ label for sugar beet and canola indicates application rates in ounces/acre. Application rates should be in fluid ounces/acre. The petitioner should submit a revised Section B.

4.2 Dietary Exposure

4.2.1 Food Exposure

Nature of the Residue - Plants and Animals (OPPTS GLN 860.1300)

Plants: The nature of the residue is considered to be understood in genetically unaltered lettuce, soybeans, corn, apples and wheat. After application of ^{14}C glufosinate ammonium to the nutrient medium (water or soil) in which these crops were grown, only one labeled metabolite could be identified, 3-methylphosphinico propionic acid. The residues of concern in/on commodities derived from genetically unaltered lettuce, soybeans, corn, apples and wheat are glufosinate ammonium and 3-methylphosphinico propionic acid (PP#8F3607, J. Garbus, 8-Aug-1990).

The nature of the residue is considered to be understood in transgenic field corn and transgenic soybeans. After application of ^{14}C glufosinate ammonium to these crops, the major residues identified were glufosinate ammonium, N-acetyl glufosinate and 3-methylphosphinico propionic acid. The residues of concern in/on commodities derived from the transgenic varieties of field corn and soybean are glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate (D211531 and D219069, M. Rodriguez, 7-Mar-1996).

In support of the requested registration, the petitioner submitted metabolism studies performed on transgenic sugar beets and transgenic canola.

Transgenic Sugar Beets: The nature of the residue in transgenic sugar beets is considered to be understood. Transgenic sugar beets were treated twice with C^{14} glufosinate ammonium at 1.0x the proposed maximum single rate (total applied was 1.0x the proposed maximum seasonal). Samples collected 0 and 21 days following the second application, and at maturity (146 days following the second application) were divided into tops and roots and analyzed. For all samples, glufosinate ammonium, N-acetyl glufosinate and 3-Methylphosphinico-propionic acid accounted for 93-98% of the total radioactive residue (TRR).

The current tolerance expression for commodities derived from transgenic crops includes the major residues identified in the transgenic sugar beet metabolism study and is therefore adequate. The residues of concern in/on commodities derived from transgenic sugar beets are glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate.

Transgenic Canola: The nature of the residue in transgenic canola is considered to be understood. Transgenic canola was treated once with C^{14} glufosinate ammonium at 0.8x the proposed maximum seasonal rate. Samples were collected 1-hour post treatment (whole plant), 21-day post-treatment (separated into top growth and roots) and at maturity (120 days after treatment; separated into roots, top growth and seed).

In the whole plant harvested 1-hour post-treatment, glufosinate ammonium and N-acetyl glufosinate accounted for 91% of the TRR. In foliage harvested 21 days post-treatment, 88% of the TRR was identified as N-acetyl-glufosinate, glufosinate ammonium and 3-methylphosphinico propionic acid. In mature canola seed, 37-55% of the TRR was identified as glufosinate ammonium, N-acetyl glufosinate and 3-methylphosphinico propionic acid and 12% of the TRR was associated with water soluble polysaccharides and proteins. In canola seed hulls, 50-59% of the TRR was identified as glufosinate ammonium, N-acetyl glufosinate and 3-methylphosphinico propionic acid.

The submitted study is marginally adequate to describe the nature of the residue in transgenic canola. The storage interval prior to analysis and extraction of whole plant and canola foliage (19 months) was not within the validated time interval (12 months). Seed and hull samples were analyzed using two HPLC systems (whole plant and foliage samples analyzed by system 1 only). Different levels of parent, N-acetyl glufosinate and 3-methylphosphinico propionic acid were observed depending on which HPLC system was used. No explanation for this difference was provided. Since adequate metabolism studies on transgenic field corn and soybean have been previously submitted (D211531 and D219069, M. Rodriguez, 7-Mar-1996) and the results from the canola study do not significantly differ from these studies, no additional data pertaining to the metabolism of glufosinate-ammonium in transgenic canola are required. The residues of concern in/on transgenic canola are glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate.

Potatoes: A metabolism study has not been performed on a genetically unaltered root vegetable (potato). Since the metabolism of glufosinate ammonium is consistent in four diverse crop groups (lettuce [leafy vegetable], soybeans [legume vegetable], wheat [cereal grain] and apple [fruit]) the nature of residues in potatoes will be considered to be understood. The residues of concern in/on potatoes are glufosinate ammonium and 3-methylphosphinico propionic acid.

Animals: The nature of glufosinate ammonium residues in lactating goats and laying hens is considered to be understood. It was shown that glufosinate ammonium and its metabolite (3-methylphosphinico propionic acid) are largely excreted and do not accumulate to any great degree in animal tissues. The only identifiable compounds in feces, urine, milk, eggs and tissues were the parent and 3-methylphosphinico propionic acid. The residues of concern in commodities derived from ruminants and poultry are glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid (PP#8F3607, J. Garbus, 8-Aug-1990).

Feed commodities derived from transgenic crops contain a second metabolite, N-acetyl glufosinate, which may lead to secondary residues of this compound in animal commodities. Feeding studies conducted on dairy cows and laying hens were submitted and reviewed as part of a glufosinate ammonium registration on transgenic field corn and soybeans (D211531 and D219069, M. Rodriquez, 7-Mar-1996). In these studies, dairy cows and hens were fed a diet consisting of 15% glufosinate ammonium and 85% N-acetyl glufosinate. Using the residues found in these feeding studies and the maximum theoretical dietary burden to ruminants and poultry, tolerances at the limit of quantitation were sufficient. Since an increase in ruminant tolerances was not necessary, it was decided that the current tolerance expression of glufosinate ammonium and 3-methylphosphinico propionic acid is adequate (inclusion of N-acetyl glufosinate ammonium was not necessary; D211531 and D219069, M. Rodriguez, 7-Mar-1996). Additionally, the tolerance expression for poultry commodities (new tolerance as a result of registration on transgenic soybeans and transgenic field corn) would include glufosinate ammonium and 3-methylphosphinico propionic acid (N-acetyl glufosinate should not be included; D232571, M. Rodriguez).

If any future petition results in a maximum theoretical dietary burden which requires milk, egg or tissue tolerances above the LOQ; the tolerance expression will be amended to include N-acetyl glufosinate.

Residue Analytical Methods (OPPTS GLN 860.1340)

Analytical methodology is available in PAM II for determination of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid in genetically unaltered apples, bananas, grapes and tree nuts (HRAV-5A) and in milk, eggs and the tissues of ruminants and poultry (HRAV-12, also called BK/01/95). In transgenic crops a second metabolite, N-acetyl glufosinate, is present. Method AE-24, which is a variation of HRAV-5A, was developed for individual determination of the three compounds regulated in transgenic crops.

Several variations of HRAV-5A and AE-24 were used for quantitation of residues in the submitted field trials; all of which are adequate for data gathering purposes. Two of these methods, BK/04/95 (used for quantitation of residues in/on transgenic sugar beet commodities) and HRAV-24 (used for quantitation of residues in/on transgenic canola commodities), were submitted to the Analytical Chemistry Branch (ACB) for Petition Method Validation (D254830, T. Bloem, 1-Apr-1999). A brief description of a GC/MS confirmatory technique has also been submitted by the registrant.

ACB has not completed the validation procedure for either method. The petitioner has provided concurrent fortification data to demonstrate that BK/04/95 and HRAV-24 are adequate for data collection purposes. HED requires a successful petition method validation and the registrant will be required to make any necessary modifications to the method resulting from petition method validation.

Multiresidue Method (OPPTS GLN 860.1360)

Glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate were not quantitatively recovered from any of the FDA Multiresidue Testing Protocols. This information has been forwarded to FDA (PP#8F3607, J. Garbus, 14-Aug-1988; PP#5F4578, M. Rodriguez, 10-Oct-1995).

Storage Stability Data (OPPTS GLN 860.1380)

The submitted storage stability study indicates that glufosinate ammonium, N-acetyl glufosinate and 3-methylphosphinico propionic acid are stable in transgenic sugar beet tops and roots for 24 months.

Previously submitted and reviewed storage stability data indicate that glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid are stable for 24 months in apples, corn grain and soybeans (PP#8F3607, J. Garbus, 8-Aug-1990). Glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate are stable for 12 months in transgenic soybean seed, forage and hay; for 3 months in soybean oil and meal; for 6 months in transgenic corn grain, fodder and forage; and for 3 months in eggs, liver, kidney and muscle (D211531 and D219069, M. Rodriguez, 7-Mar-1996).

These storage intervals are adequate to cover the submitted field trial data (excluding sugar beet processed commodities; see processed food section).

Meat and Milk, Poultry and Eggs (OPPTS GLN: 860.1480)

Two dairy cow and two poultry feeding studies have been previously submitted, reviewed and determined to be adequate: **(1)** dairy cows and poultry feed a diet containing a 3:1 mixture of glufosinate ammonium and 3-methylphosphinico propionic acid (PP#8F3607, J. Garbus, 8-Aug-1990) and **(2)** dairy cows and poultry feed a diet containing 15% glufosinate ammonium and 85% N-acetyl glufosinate (D211531 and D219069, M. Rodriguez, 7-Mar-1996). Since the majority of the dietary burden to ruminants and poultry originates from transgenic crops, the feeding studies performed with N-acetyl glufosinate and glufosinate ammonium will be considered representative. Considering all registered and proposed uses, the maximum theoretical dietary burden to ruminants and poultry requires no adjustment to the currently established tolerances.

Crop Field Trials (OPPTS GLN 860:1500)

Transgenic Sugar Beets: The two submitted sugar beet field trial studies are acceptable. The combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate in/on transgenic sugar beet tops and roots treated with Liberty™ Herbicide at 1.0-1.3x the maximum proposed seasonal rate ranged from <0.10 - 1.30 ppm (tops) and <0.10 - <0.830 ppm (roots). HED concludes that based on the submitted field trial data, the appropriate tolerance in/on sugar beet tops and roots is 1.5 ppm and 0.9 ppm, respectively.

Transgenic Canola: The two submitted canola field trial studies are acceptable. The combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate in/on transgenic canola seed following a single application of glufosinate ammonium at 0.8-1.2x the maximum proposed seasonal rate ranged from <0.15 - <0.336 ppm. HED concludes that based on the submitted field trial data, the appropriate tolerance in/on canola seed of 0.4 ppm, is appropriate.

Potatoes: The submitted potato field trial study is acceptable. The combined residues of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid in/on potatoes treated with Rely® Herbicide at 1.1x the maximum proposed seasonal rate ranged from <0.10 - <0.667 ppm. HED concludes that based on the submitted field trial data, the appropriate tolerance in/on potatoes is 0.8 ppm.

Processed Food/Feed (OPPTS GLN: 860.1520)

Transgenic Sugar Beet: Sugar beets treated with Liberty™ Herbicide at 7.2x the maximum proposed seasonal application rate were harvested and processed into pulp, molasses and sugar. The combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate did not concentrate in pulp or sugar but did concentrate 6.8x in molasses. Processed samples were stored for 3 months prior to analysis. No storage stability data for sugar beet pulp, molasses or sugar have been submitted. The maximum combined glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate residue expected in sugar beet molasses, based on the highest average field trial (HAFT; 0.719 ppm; Fayette, OH; MRID 44358603) and the 6.8x concentration factor, is 5.0 ppm.

HED will not be opposed to conditional registration of glufosinate ammonium on transgenic sugar beets. Unconditional registration may be granted upon validation of the three-month storage interval for the processed commodities (sugar, pulp and molasses). Pending submission and evaluation of this data, HED concludes that the appropriate sugar beet molasses tolerance is 5.0 ppm.

Transgenic Canola: Canola seed harvested 70 days after treatment with glufosinate ammonium at 0.8x, 1.5x and 3.0x the maximum proposed seasonal application rate, were processed into meal, oil and soapstock. The combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate did not concentrate in oil or soapstock but did concentrate 3.4x and 2.9x in toasted meal (average 3.2x). HED concludes that based on the highest field trial residue (<0.336 ppm; Indian Head, Sk; MRID 44358609) and 3.2x concentration factor, the appropriate canola meal tolerance is 1.1 ppm.

Potato: Potatoes harvested 9 days after a single treatment with glufosinate ammonium at 5.3x the maximum proposed single and seasonal application rate were processed into chips, flakes and peel. Glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid did not concentrate in potato peel but did concentrate 2.3x in potato chips and 3.0x in potato flakes. HED concludes that based on the HAFT (0.662 ppm;Lee, FL; MRID 44583901) and the concentration factors the appropriate potato flake/granule and potato chip tolerances are 2.0 ppm and 1.6 ppm, respectively.

Confined/Field Accumulation in Rotational Crops (OPPTS GLN: 860.1850 & 860.1900)

The submitted label indicates a 120-day plant back interval for wheat only. The label must be changed to indicate a 120-day plant back interval for all crops except wheat where a 70-day plant back interval is appropriate (D211531 and D219069, M. Rodriguez, 7-Mar-1996; P. Errico [RD], 6-May-1998).

International Harmonization of Tolerances

Codex currently has maximum residue limits (MRLs) for the combined residues of glufosinate ammonium and 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents in/on potatoes and sugar beets at 0.5 and 0.05 ppm, respectively (no MRLs established for canola). Canada currently has MRLs for the combined residues of glufosinate ammonium and 3-methylphosphinico propionic acid in/on potatoes and canola at 0.4 ppm and 3.0 ppm, respectively (no MRLs established for sugar beets). No glufosinate ammonium MRLs have been established in/on potatoes, sugar beets or canola in Mexico.

Since the Canadian MRL for canola seed is significantly greater than the appropriate US tolerance, harmonization is not possible. Since the appropriate US tolerance for sugar beets and potatoes are greater than the Canadian and Codex MRLs, harmonization is not possible.

Dietary Risk Analysis

A chronic and acute dietary exposure analysis, using the Dietary Exposure Evaluation Model (DEEM™), was completed (D257266, T. Bloem, 19-Jul-1999; Attachment 4). Both the acute and chronic DEEM™ analyses used consumption data from USDA's 1989-1992 nationwide Continuing Survey for Food Intake by Individuals (CSFII).

Acute: The acute dietary exposure analysis for females 13 - 50 (no acute dietary endpoint was identified for the general US population including infants and children) assumed tolerance level residues and 100% crop treated for all registered and proposed commodities (Tier 1 analysis). The most highly exposed population was females 13 - 50/nursing at 58% of the aPAD (95^{th} percentile). Acute dietary food exposure to glufosinate ammonium is below HED's level of concern.

Table 4: Summary of Results from Acute DEEM™ Analysis for Glufosinate Ammonium

subgroups	exposure[1] (mg/kg/day)	% aPAD[2]
Females (13 - 50, preg., not nursing)	0.008179	39
Females (13 - 50, nursing)	0.012131	58
Females (13-19 yrs., not preg., not nursing)	0.008425	40
Females (20+ years, not preg., not nursing)	0.007086	34
Females (13-50 years)	0.007751	37

1 95th percentile exposures
2 aPAD = 0.021 mg/kg/day

Chronic: The chronic dietary exposure analysis assumed tolerance level residues for all registered and proposed commodities. The weighted average percent crop treated was incorporated for all registered commodities (sweet corn maintained at 100%; Tier 2 analysis). The most highly exposed population was children 1-6 years old at 71% of the cPAD. Chronic dietary food exposure to glufosinate ammonium is below HED's level of concern.

Table 5: Summary of Results from Chronic DEEM™ Analysis for Glufosinate ammonium

subgroups[1]	exposure (mg/kg/day)	% cPAD[2]
U.S. Population (48 states)	0.002120	30
Non-Hispanic blacks	0.002246	32
Non-Hispanic/non-white/non-black	0.002256	32
Non-Hispanic whites	0.002132	31
Children (1-6 years)	0.004974	71
Females (13 - 50 nursing)	0.002035	29
Males 13-19 yrs	0.002449	35

1 The subgroups listed above are the US Population and other general subgroups for which the %cPAD is greater than that of the US Population
2 cPAD = 0.007 mg/kg/day

4.2.2 Water Exposure

The following information was provided by EFED (D250756 & D257381, E. L. Libelo, Attachment 5). At the present time, there are no surface or ground water monitoring data available.

Environmental Fate Assessment: Glufosinate ammonium is highly water soluble and stable to hydrolysis and photolysis. Aerobic soil, anaerobic soil and aerobic aquatic half-lives are 23, 56 and 35 days, respectively. The relatively short half-lives for glufosinate ammonium are such that a sustained concentration in surface water is not likely. Due to the high water solubility of glufosinate ammonium, it will reach ground water relatively quickly and thereby counteract the degradation seen in surface water. No information pertaining to the environmental fate of the 3-methylphosphinico propionic acid was provided by the petitioner. Ground and surface water concentration estimates were generated using the highest registered and proposed application rate for glufosinate ammonium (apples; 1.5 lbs ai/application; 4.5 lbs ai/year), the SCI-GROW screening model for ground water (Tier 1), and the PRZM/EXAMS model for surface water (Tier 2).

ground water estimate:	1.16 µg/L
surface water estimates:	34.1 µg/L (1 day in 10 year maximum) 0.79 µg/L (36 year average daily concentration)

Drinking Water Risk (acute and chronic): Aggregate exposures are generally calculated by summing dietary (food and water) and residential exposures. If the aggregate exposure is less than the specified PAD, the exposure is not expected to be of concern. Since HED does not have ground and surface water monitoring data to calculate a quantitative aggregate exposure, DWLOCs were calculated. The DWLOC is the upper limit of a chemical's concentration in drinking water that will result in an acceptable aggregate exposure. The DWLOC is used as a point of comparison against model estimates of a pesticide's concentration in water. DWLOC values are not regulatory standards for drinking water. They do have indirect regulatory impact through aggregate exposure and risk assessments.

To calculate the acceptable acute and chronic exposure to glufosinate ammonium in drinking water, the dietary food exposure estimate was subtracted from the appropriate PAD (only short-term residential exposure). A DWLOC was then calculated by using default body weights and drinking water consumption figures (70kg/2L (adult male), 60kg/2L (adult female) and 10kg/1L (infant/child)).

The estimated maximum and average concentration of glufosinate ammonium in ground and surface water are less than HED's DWLOC for glufosinate ammonium as a contribution to acute and chronic aggregate exposure (for all population subgroups). EFED believes that the SCI-GROW model underestimates the potential glufosinate ammonium concentration in ground water. The DWLOCs are a minimum of 17x greater than the SCI-GROW model estimates. Therefore, an adequate margin of safety is present. Tables 6 and 7 are summarizes of acute and chronic DWLOCs.

Table 6: Acute DWLOCs

Population Subgroup[1]	aPAD mg/kg/day	Food Exposure mg/kg/day	Maximum Water Exposure[2] mg/kg/day	DWLOC[3] ppb	SCI-GROW ppb	PRZM-EXAMS ppb
Females (13 - 50, nursing)	0.021	0.012131	0.008869	270	1.16	34.1

[1] highest exposed subgroup among females 13 - 50
[2] maximum water exposure (mg/kg/day) = 0.021 mg/kg/day - acute food exposure (mg/kg/day)
[3] DWLOC = [(maximum water exposure mg/kg/day)(body weight kg)/(water consumption liters)] * 1000

Table 7: Chronic (non-cancer) DWLOC

Population Subgroup[1]	cPAD mg/kg/day	Food Exposure mg/kg/day	Maximum Water Exposure[2] mg/kg/day	DWLOC[3] ppb	SCI-GROW ppb	PRZM-EXAMS ppb
US Population	0.007	0.002120	0.004880	170	1.16	0.79
Non-Hispanic blacks	0.007	0.002246	0.004754	170	1.16	0.79
Non-Hispanic/non-white/non-black	0.007	0.002256	0.004744	170	1.16	0.79
Non-Hispanic whites	0.007	0.002132	0.004868	170	1.16	0.79
Children 1-6 yrs	0.007	0.004974	0.002026	20	1.16	0.79
Females 13 - 50 nursing	0.007	0.002035	0.004965	150	1.16	0.79
Males 13-19 yrs	0.007	0.002449	0.004551	160	1.16	0.79

[1] The subgroups listed above are the following: (1) US Population, (2) the other general subgroups for which the %cPAD is greater than that of the US Population and (3) the most highly exposed population among infants and children, females, and males.
[2] maximum water exposure (mg/kg/day) = (0.007 mg/kg/day - acute food exposure, (mg/kg/day)); no residential exposure
[3] DWLOC = [(maximum water exposure mg/kg/day)(body weight kg)/(water consumption liters)] * 1000

4.3 Occupational Exposure

The worker exposure and risk assessment presented in this document are based on the Pesticide Handler Exposure Database Version 1.1 (PHED, Surrogate Exposure Guide, August 1998) unit exposure estimates for workers wearing long pants, long sleeves, gloves (no gloves for aerial applicators), and using open cab ground equipment, and closed cab aerial equipment. There are no chemical specific data available to determine the potential risks associated with the proposed uses of glufosinate ammonium on transgenic canola, sugarbeets, and for desiccation of conventional potato vines.

Table 8: Use Pattern and Formulation Information

Formulation Type, % ai	Equipment	Use Sites	Application rate range	Timing and frequency of applications	Comments
Liquid 18.19% ai	ground and aerial equipment	transgenic sugarbeets, canola	**sugarbeets:** 0.26 - 0.55 lb ai/acre; not to exceed 1.1 lbs ai/acre/growing season **canola:** 0.26 - 0.42 lb ai/acre; not to exceed 0.89 lbs ai/acre/growing season	**sugarbeets**: 3 X season; from the cotyledon stage up to 10 leaf stage; PHI= 60 days **canola:** 2 X season; from the cotyledon stage up to the early bolting stage repeat applications should be made when newly germinated weeds again reach 1 inch in height or diameter; PHI = 65 days	foliar active material with no soil-residual activity; rainfast 4 hrs. after application; to be applied to young, actively growing weeds
Liquid 11.3% ai		potatoes	0.38 lb ai/acre	apply at the beginning of natural senescence of potato vines; PHI= 9 days	

4.3.1 Handler

Exposure Assumptions: The exposure assessment is based on the crop with the highest application rate (sugarbeets) and the crop with the highest average farm size (canola), as a conservative scenario. Commercial mixer/loaders (for aerial applications), commercial applicators (groundboom and aerial), and farmers (groundboom) treating their own fields were chosen as the most conservative scenarios. The occupational exposure assessment is based on the assumptions listed in Table 9.

Table 9: Assumptions for Worker Exposure Assessments

Exposure Scenario[1]	Unit Exposure ug/lb ai[2]		Application rate (lb ai/A)	Acres/ Day[3]	Data source
	Dermal	Inhalation			
Mixer/Loader (aerial)	23	1.2	0.55	570	Unit exposures: Pesticide Handlers Exposure Database V1.1, Surrogate Exposure guide, August 1998. Estimates for all liquids, open mixing/loading; high confidence data
Applicator (groundboom - open cab)	14	0.7	0.55	380	Estimates for groundboom, open cab; medium confidence data
Applicator (aerial - enclosed cockpits)	5	0.068	0.55	570	Estimates for aerial/fixed-wing/closed cab/liquid; medium confidence data
Mixer/loader and applicator (groundboom)	37	1.9	0.55	190	Unit exposures were estimated by adding the M/L and applicator unit exposures

1 Handlers wearing long-sleeved shirt, long pants, and gloves (no gloves for aerial applicators)
2 Pesticide Handler Exposure Database Version 1.1 (PHED, Surrogate exposure Guide, August 1998)
3 Average canola farm is approximately 190 acres (United States 1997 Census of Agriculture, Table 42). Ground applicator assumed to treat 2 farms/day, aerial applicator assumed to treat 3 farms/day. The highest application rate and acreage from the proposed uses were used in this assessment.

Worker Exposure and Risk Assessment: Table 10 summarizes the worker exposure and risk estimates for commercial mixer/loaders, commercial applicators, and for farmers (m/l/a) treating their own fields. Short and intermediate-term exposures are expected for commercial applicators; only short-term exposures are expected for private applicators. Since workers are required to wear additional personal protective clothing (coveralls and protective eyewear) that are not accounted for in this assessment, the estimates of exposure are considered conservative.

Table 10: Occupational Exposure and Risk Estimates

Exposure Scenario	Unit Exposure (ug/lb ai)		Exposure[1] (mg/kg/day)			Short- & Intermediate - Term MOE[2]		
	Dermal	Inhalation	Dermal	Inhalation		Dermal	Inhalation	
				Short	Intermediate		Short	Intermediate
Mixer/ Loader	23	1.2	0.10	0.0054	0.0063	1000	1000	390
Applicator Groundboom - open cab	14	0.7	0.042	0.0021	0.0024	2400	3000	880
Applicator Aerial - enclosed cockpits	5	0.068	0.022	0.00031	0.00036	4600	20000	5800
Mixer/loader applicator (groundboom)	37	1.9	0.055	0.0028	0.0033	1800	2300	640

1 Exposure = Unit exposure × application rate × acres/day × 1/kg bw × .001mg/ug; 60 kg bw for short-term inhalation exposure, 70 kg bw for other exposures
2 Dermal NOAEL = 100mg/kg/day; Inhalation NOAEL = 6.3mg/kg/day and 2.1mg/kg/day for short-term exposure and intermediate- term exposures, respectively. MOE = NOAEL÷ Exposure; Level of concern = 100

The potential risks for occupational workers from short and intermediate-term exposures from the proposed uses of glufosinate ammonium on canola, sugarbeets, and potatoes do not exceed the Agency's level of concern. Chronic exposures are not expected from the proposed uses, therefore a risk assessment was not conducted.

4.3.2 Post-Application

There are no chemical-specific data available to determine the potential risks from post application activities associated with this proposed section 3 use of glufosinate ammonium. However, potential post-application exposures are not of concern, based on the use pattern, timing of applications, and the fact that planting and harvesting of the subject crops are mechanized. Most workers entering treated fields are likely to be performing low contact labor tasks such as mechanical incorporation and cultivation. Hoeing and scouting activities are also anticipated, but risks from these activities are not expected to exceed the Agency's levels of concern. For the purposes of the proposed use, reentry restrictions and personal protective clothing specified on the product label should provide adequate protection from the potential post-application exposures. Workers reentering treated fields before the required restricted entry interval are required to wear coveralls over short-sleeved shirts and short pants, chemical-resistant gloves, chemical resistant footwear and socks, and protective eyewear.

Restricted Entry Interval (REI): The interim restricted entry interval (REI) is 12 hours based on glufosinate ammonium's acute toxicity classification III for the dermal, inhalation, and ocular routes of exposure.

4.4 Residential Exposure

Glufosinate ammonium is registered for residential (outdoor, non-food) products as a non selective, postemergent herbicide. As such, it is primarily used as a spot treatment around trees, shrubs, fences, walks, patios, driveways, sidewalks, and flower beds. It is also registered for lawn renovation uses. There is no chemical specific data to assess exposures from the registered residential uses of glufosinate ammonium. The HED Exposure SAC considered these uses and recommended that the turf and garden scenarios, as specified in the Draft HED Standard Operating Procedures (SOPs) for Residential Exposure Assessments (18-DEC-1997), be used as a screening level assessment of the potential risks to homeowners from glufosinate ammonium use (see attachment 7, ***Minutes for Meeting of the Science Advisory Council for Exposure***).

4.4.1 Handler/Post-Application

The risk assessment was conducted using the following assumptions: dermal and inhalation unit exposure of 100 mg/lb ai and 30 ug/lb ai, respectively, maximum application rate of 1.4 lb ai/acre (product label), and a maximum area treated of 10,000 sq. ft. for the garden use scenario, 20,000 sq ft for the lawn renovation scenario, and 1,000 sq ft for "spot" lawn renovation scenario. Intermediate- and chronic-term residential exposures are not expected from the registered uses of glufosinate ammonium, therefore only short-term exposures were considered.

Table 11: Residential Handler Exposure and Risk Assessment

Scenario	Unit Exposure (mg/ lb ai)		Potential Dose Rate[1] (mg/kg/day)		Short -Term MOE[2]	
	Dermal	Inhalation	Dermal	Inhalation	Dermal	Inhalation
Garden use (low pressure hand wand)	100	0.030	0.46	1.4 E-4	*217*	45,000
Lawn renovation (full lawn; garden hose end sprayer)	30	0.0095	0.28	1.0 E-4	*360*	63,000
Lawn renovation (spot treatment; low pressure hand wand)	100	0.030	0.046	1.4 E-5	2200	450,000

1 Potential Dose Rate (PDR) = Unit exposure x Maximum application rate (1.4 lbs ai/acre) x Maximum area treated (garden use:10,000sq ft; lawn renovation: 20,000sq ft for full lawn and 1,000sq ft for spot treatment) ÷ kg bw (70 kg bw and 60 kg bw for short-term dermal and inhalation exposure, respectively. (Draft HED Standard Operating Procedures (SOPs) for Residential Exposure Assessments and Appendix B (18-DEC-1997)

2 Dermal NOAEL = 100 mg/kg/day; Inhalation NOAEL = 6.3 mg/kg/day for Short-term exposure; MOE = NOAEL/Exposure; Level of concern = 300

Table 12: Residential Post-Application Exposure and Risk Assessment [1]

Scenario	Transfer coefficient (cm^2/hr)	Potential Dose Rate[2] (mg/kg/day)	MOE[3]
Adult (garden use)	10,000	0.3	330
Children (garden use)	5,000	0.13	770
Adult (lawn renovation)	43,000	0.96	100
Children (lawn renovation)	8,700	0.91	110

1 Draft HED Standard Operating Procedures (SOPs) for Residential Exposure Assessments and Appendix B 18-DEC-1998). DFR_0 = Application rate x fraction available as residue (20% for garden use, 5% for lawn use: based on a decision of the Science Advisory Council for Exposure, see Minutes for Meeting of the Science Advisory Council for Exposure dated August 5, 1999) x 4.54E8 ug/lb x 2.47E-8 acre/cm^2 = 3.14 ug/cm^2 for garden use; 0.78 for lawn use

2 Potential post application dose rate= DFR x Transfer coefficient x Exposure time (garden use: 0.67 hr/ for adults, 0.33 hrs for children; lawn use: 2.0 hr) / BW (70 kg for adult, 39.1 for children (garden use) and 15 kg for children (lawn use) x 0.001mg/ug

3 Dermal NOAEL = 100 mg/kg/day; MOE = NOAEL/Exposure; Level of concern = 300

These estimates indicate that the potential risks from homeowner uses of glufosinate ammonium exceed the Agency's level of concern. The Agency's level of concern is for MOEs below 300. The dermal MOEs for homeowners applying glufosinate ammonium for the garden use is 217. The dermal MOEs for postapplication exposures from lawn renovation uses are 100 and 110 for adults and children, respectively. These estimates are based on screening level assumptions and therefore should be considered conservative.

In looking at these risk estimates it should be kept in mind that: **(1)** residential use of nonselective herbicides is likely to occur as a "spot spray" in small turf areas with a high content of non-desirable grasses or in areas that have been converted to some other uses such as vegetable or flower gardening. Lawn renovation treatment is recommended when 70% of the lawn is infested with undesirable lawn grasses (***Renovating your lawn, publication from Rutgers Cooperative Extension Service, N.J. Agricultural Experiment Station***). Therefore lawn renovation is considered a "last resort" treatment and a use pattern that is not likely to involve the average homeowner on a regular basis (scheduled treatments with selective herbicides to control undesirable weeds); **(2)** Information from Turfgrass Producers International (a not-for-profit trade association) indicates that "80% of nonselective herbicides production is used on new construction, with the remaining 20% going to golf courses, parks, sports fields, cemeteries, roadsides, etc. Exceptionally small amounts of turfgrass sod are used in lawn restoration projects"; **(3)** Information from AgrEvo indicates that sales of formulations containing glufosinate ammonium (Finale® Concentrate and Super Concentrate) sold to the homeowner lawn and garden market in 1998 represents a very small percentage of that for crops. It should also be considered that the SOP's assumptions for the garden scenario are based on a 10,000 sq ft "farm garden" which is not representative for the average homeowner. In addition, the lawn renovation scenario is based on transfer coefficients and assumptions used for regular lawn uses which are not necessarily applicable to lawn renovation uses and therefore, further overestimate the real potential risks.

5.0 AGGREGATE EXPOSURE AND RISK ASSESSMENT/CHARACTERIZATION

5.1 Acute Aggregate Risk

The acute dietary exposure analysis for females 13 - 50 (no acute dietary endpoint was identified for the general US population including infants and children) assumed tolerance level residues and 100% crop treated for all registered and proposed commodities (Tier 1 analysis). The most highly exposed population among females 13 - 50 was nursing females at 58% of the aPAD (95th percentile). The estimated glufosinate ammonium concentration in surface and ground water are less than HED's DWLOC (for all population subgroups). Acute aggregate exposure to glufosinate ammonium, as a result of all registered and proposed uses, is below HED's level of concern.

5.2 Short- and Intermediate-Term Aggregate Risk

Short- and intermediate-term aggregate risk assessments include average dietary exposure (food and water) and short- or intermediate-term dermal and inhalation exposures from residential uses. The dermal exposure estimates from the registered residential uses of glufosinate ammonium are above HED's level of concern (inhalation residential exposures were insignificant). According to HED policy (HED SOP 97.2), the residential dermal exposures cannot be aggregated with chronic dietary exposure because different endpoints were chosen for these exposure scenarios.

5.3 Chronic Aggregate Risk

There are no chronic residential exposure scenarios. Therefore, only food and water are included in the chronic aggregate risk. The chronic dietary exposure analysis assumed tolerance level residues for all registered and proposed commodities and incorporated the weighted average percent crop treated (BEAD, A. Halvorson, 15-Apr-1999) for all registered commodities (sweet corn maintained at 100% crop treated; Tier 2 analysis). For the most highly exposed subgroup (children, 1-6 years), 71% of the cPAD is occupied by dietary (food) exposure. The estimated glufosinate ammonium concentrations in surface and ground water are less than HED's DWLOC (for all population subgroups). Chronic aggregate exposure to glufosinate ammonium, as a result of all registered and proposed uses, is below HED's level of concern.

5.4 Cancer Aggregate Exposure and Risk

Glufosinate ammonium has been classified as a **"not likely"** carcinogen according to the EPA *Proposed Guidelines for Carcinogen Risk Assessment*. Therefore, a cancer risk assessment is not necessary.

6.0 ACTIONS REQUIRED BY REGISTRANTS

6.1 Data Requirements

6.1.1 Toxicology Studies :

- Acute Neurotoxicity, Subchronic Neurotoxicity and Developmental Neurotoxicity Studies (Guidelines 81-8, 82-7 and 83-3; respectively)

6.1.2 Chemistry

- A Revised Section B (Liberty™, Rely®)
- Storage stability Study for Sugar Beet Processed Commodities (sugar, pulp and molasses; 3 months) (Guideline 860.1380)
- Petition Method Validation for Methods BK/04/95 (sugar beets) and HRAV-24 (canola). Validation of these methods has been requested (D254830, T. Bloem, 1-Apr-1999) but has not been completed. The petitioner has provided concurrent fortification data to demonstrate that BK/04/95 and HRAV-24 are adequate for data collection purposes. HED requires a successful petition method validation and the registrant will be required to make any necessary modifications to the method resulting from petition method validation.

6.1.3 Occupational/Residential: None

cc without attachments: PP#s 7404910 & 8F04997, Myrta Christian, Myron Ottley, Tom Bloem
RDI: M. Morrow (8-Sep-1999), RAB1 (6-Aug-1999), RARC (17-Aug-1999)
T. Bloem:806R:CM#2:(703)605-0217

013728

Attachment 1: Report of the Hazard Identification Assessment Review Committee. 17-MAY-1999

HED Doc. No. 013385, M. Ottley, 17-May-1999

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

HED DOC. NO. 013385

DATE: 17-MAY-1999

MEMORANDUM

SUBJECT: *GLUFOSINATE AMMONIUM* - Report of the Hazard Identification Assessment Review Committee.

FROM: Myron S. Ottley
Registration Action Branch 1
Health Effects Division (7509C)

THROUGH: Jess Rowland, Co-Chairperson
Hazard Identification Assessment Review Committee
Health Effects Division (7509C)

Pauline Wagner, Co-Chairperson
Hazard Identification Assessment Review Committee
Health Effects Division (7509C)

TO: Melba Morrow, Branch Senior Scientist
Registration Action Branch1
Health Effects Division (7509C)

PC Code: 128850

On May 5, 1999, the Health Effects Division's Hazard Identification Assessment Review Committee evaluated the toxicology data base of **Glufosinate ammonium,** established an acute Reference Dose and reestablished the chronic Reference Dose and addressed the potential enhanced sensitivity of infants and children as required by the Food Quality Protection Act (FQPA) of 1996.

Committee Members in Attendance

Members present were: Jess Rowland, Kathleen Raffaele, Nicole Paquette, Virginia Dobozy, Sue Makris, David Anderson, PV Shah, Karen Hamernik, and Brenda Tarplee (Executive Secretary). Member(s) in absentia: William Burnham and Nancy McCarroll. Data were presented by Myron S. Ottley of RAB1. Other RAB1 personnel in attendance, Melba Morrow (BSS), Myrta Christain Odiott (exposure assessor) and Thomas Bloem (chemist).

Data Presentation:
and
Report Presentation

____
Myron S. Ottley
Pharmacologist

I. INTRODUCTION

Chemical Name: Glufosinate Ammonium **Ignite® Herbicide**

Synonyms: HOE 039866, DL-glufosinate ammonium

Isomers: HOE 058192 L-Isomer

Metabolites: HOE 099730 n-acetyl glufosinate
HOE 061517 3-methylphosphinico propionic acid
HOE 042231 disodium 2-hydroxy-4-methylphosphinato butyrate (IUPAC)

Current Actions:

1. Section 3 registration for transgenic sugar beet and canola,
2. Import tolerance for potato
3. Expiring Tolerances for almonds, apples, and grapes, tree nut group.

II. HAZARD IDENTIFICATION

A1. Acute Reference Dose (RfD) (females 13+ only)

Study Selected: Developmental Toxicity–Rabbit §83-3b

MRID No.: 41144703

Executive Summary: In a developmental toxicity study groups of 15 pregnant female Himalayan rabbits were administered by gavage HOE 039866 at doses of 0., 2.0, 6.3 or 20.0 mg/kg/day from days seven to 19 of pregnancy.

There was a decrease in body weight (6 - 8%, $p \leq 0.05$), body weight gain (37%, $p \leq 0.05$) and food consumption (39%, $p \leq 0.05$) in 20 mg/kg dams. A drop in food consumption (15%, $p \leq 0.05$) was also seen at 6.3 mg/kg. In the 20 mg/kg group, there were increased kidney weights (11%, $p \leq 0.05$) in the dams. Also at 20 mg/kg/day there was an increase in the number of dead fetuses/litter (0.55/litter vs. 0.00/litter in controls, reported as outside the normal range") and a 4% decrease in mean fetal body weight, also reported as "outside the normal range". Increased incidence of incomplete or absent ossification of skeletal bones in fetuses were observed in the 6.3 and 20.0 mg/kg groups (3 fetuses in 2 litters at 6.3 mg/kg, 9 fetuses in 4 litters at 20 mg/kg. Statistical analysis was not reported).

Based on the findings presented in this report, the **NOAEL for maternal toxicity was 2.0 mg/kg/day. The LOAEL is 6.3 mg/kg/day based on reduced food consumption, body weight and weight gains and increased kidney weights. The developmental NOAEL was 6.3 mg/kg/day based on decreased body weights and fetal death at 20 mg/kg/day.**

This study is **classified as Acceptable (Guideline)** and meets the requirements for a developmental toxicity study (83-3b) in the rabbit.

Dose and Endpoint for Risk Assessment: 6.3 mg/kg/day based on reduced fetal body weight and increased fetal death at 20 mg/kg/day.

Comments about Study/Endpoint: The fetal effects are presumed to occur after a single dose. The *in utero* effects observed are applicable only to the females 13+ subgroup, and not the general population.

Uncertainty Factor (UF): 100

Acute RfD = 0.02 mg/kg/day

This risk assessment for Acute Dietary IS required for the females 13+ subgroup only.

A2. Acute Reference Dose (RfD) (general population including infants and children)

Study Selected: None §

MRID No.: None

Executive Summary: None

Dose and Endpoint for Risk Assessment: None

Comments about Study/Endpoint: No endpoint attributable to a single exposure was identified for the general population, including infants and children.

Uncertainty Factor (UF): None

Acute RfD = None

This risk assessment for Acute Dietary IS NOT required for the general population including infants and children.

B. Chronic RfD

Study Selected: Two-year chronic toxicity/oncogenicity–Rat **§83-5**

MRID No.: 40345607, 41147701

Executive Summary: In a combined chronic toxicity/oncogenicity study (MRID 40345607, 41144701) glufosinate ammonium technical (95.3% a.i.) was administered to 50 Wistar rats/sex/dose in the diet for 30 months (carcinogenicity portion) at dose levels of 0, 40, 140, or 500 ppm (mean compound intake in males was 0, 2.1, 6.8, and 24.4 mg/kg/day and for females was 0, 2.4, 8.2 and 28.7 mg/kg/day, respectively). In addition 20 rats/sex/dose were treated for 24 months (chronic portion), and 10 rats/sex/dose were treated for 12 months (interim sacrifice).

There was increased mortality ($p \leq 0.05$) in females at 140 and 500 ppm (60, 77, 90, 97%

controls to high dose). Increased kidney glutamine synthetase activity ($p \leq 0.05$) was observed in all treated females and in mid-and high-dose males. Increased absolute and relative kidney weights ($p \leq 0.05$) were observed in mid- and high-dose males, and in all treated females (not a strong dose relation); also, increased kidney to brain weight ratio was observed in males at these dose levels. There was an 11 % inhibition of brain glutamine synthetase in 500 ppm females (male values could not be determined). **The LOAEL is 140 ppm (6.8 mg/kg/day) based on increased kidney weight and kidney/brain weight in males at 52 weeks, and decreased survival in females at 130 weeks. The NOAEL is 40 ppm (2.1 mg/kg/day).**

There was no clear demonstration of increased tumor incidence following exposure to glufosinate ammonium. Dosing was considered adequate in females based on mortality and inhibition on brain glutamine synthetase, inadequate in males.

This study is classified as acceptable (guideline), and satisfies the guideline requirement for a chronic toxicity study **(83-1a)** in rats. This study is classified as Acceptable and satisfies the guideline requirement for a cancer study **(83-2a)** in female rats. It is acceptable (guideline) only when considered in combination with the two year cancer data for male rats).

Dose and Endpoint for Establishing RfD: NOAEL of 2.1 mg/kg/day based on increased kidney weight and kidney/brain weight in males, and decreased survival in females.

Uncertainty Factor(s): 100

$$\textbf{Chronic RfD} = \frac{2.1 \text{ mg/kg/day (NOAEL)}}{100 \text{ (UF)}} = \mathbf{0.021\ mg/kg/day}$$

Comments about Study/Endpoint/Uncertainty Factor: The endpoint represents the lowest NOAEL in the most sensitive species.

This risk assessment for chronic dietary IS required.

C. Occupational/Residential Exposure

1. Dermal Absorption

Study Selected: Pharmacokinetics with dermal application in rat **§85-2**

MRID No.: 40345620

Executive Summary: Groups of male Wistar rats (28/dose level) were dermally administered radioactive HOE 039866 (glufosinate ammonium) at levels of 0.1, 1.0 or 10.0 mg/rat on 6 cm^2 of shaved skin. Four rats/dose were exposed for 0.5, 1, 2, 4, 10, 24 or 168 hrs. The quantity of radioactivity in feces, urine and various tissues was measured.

The results indicate that at the low dose (0.1 mg) 42.5 to 50.8% of the applied radioactivity was absorbed whereas at the high dose (10 mg) 26% was absorbed. After removal and washing of the treated skin a substantial amount of the radioactivity still remained in the skin, and it was gradually absorbed and eliminated. Radioactivity was found in both feces and urine samples, but the majority of HOE 039866 was eliminated in the urine. In all organs/tissues examined, radioactivity was found to reach a maximum level either at four or 10 hr after exposure. Subsequently, the radioactivity dropped rapidly. The amount of radioactivity found in the brain was very minimal relative to that of kidneys and liver.

This study is classified as ACCEPTABLE (Guideline), and satisfies the guideline requirements for a dermal penetration study (85-2).

Dermal Absorption Factor: 50%. Percentage dermal absorption is based on the range of 42.5% to 50.8% of radioactivity absorbed at 0.10 mg/kg.

2. Short-Term Dermal - (1-7 days)

Study Selected: 21-Day Dermal–Rat §82-2

MRID No.: 40345605

Executive Summary: In a 21-day repeated dose dermal toxicity study (MRID 40645605), groups of 6 male and 6 female Wistar rats were treated with HOE 039866 (glufosinate ammonium) (95.3%) in deionized water by dermal occlusion at doses of 0, 100, 300 or 1000 mg/kg/day, 6 hours/day, five days/week for 21 applications in 30 days. An additional five males and five females/dose group were dosed and observed for 44 days in a "recovery study".

Two of six low-dose males at 300 mg/kg/day, and four of 11 males and two of 11 females at 1000 mg/kg/day displayed aggressive behavior, piloerection and a high startle response. There were no effects of toxicological importance on body weights, food consumption, hematology, clinical chemistry, urinalysis, organ weights, or gross or microscopic pathology. No specific results were reported for the recovery group. **Based on clinical observations, the LOAEL is 300 mg/kg/day and the NOAEL is 100 mg/kg/day.**

This study is classified as **acceptable** and satisfies the guideline requirements for a 21-day dermal study (82-2) in rats.

Dose and Endpoint for Risk Assessment: 100 mg/kg/day based on neurological clinical signs (hyperactivity, aggressive behavior, piloerection) at the LOAEL of 300 mg/kg/day

Comments about Study/Endpoint:. These effects are seen following dermal exposure in animals, which simulates human exposure, and is appropriate for this exposure scenario.

This risk assessment IS required.

3. Intermediate-Term Dermal (7 Days to Several Months)

Study Selected: 21-Day Dermal–Rat §82-2

MRID No.: 40345605

Executive Summary: See Short-Term Dermal

Dose and Endpoint for Risk Assessment: 100 mg/kg/day based on neurological clinical signs (hyperactivity, aggressive behavior, piloerection) at the LOAEL of 300 mg/kg/day

Comments about Study/Endpoint:. These effects are seen following dermal exposure in animals, which simulates human exposure, and is appropriate for this exposure scenario.

This risk assessment IS required.

4. Long-Term Dermal (Several Months to Life-Time)

Study Selected: Two-Year Chronic Toxicity/Carcinogenicity–Rat §83-5

MRID No.: 40345607, 41147701

Executive Summary: see Chronic Dietary

Dose and Endpoint for Establishing RfD: NOAEL of 2.1 mg/kg/day based on increased kidney weight and kidney/brain weight in males, and decreased survival in females.

Comments about Study/Endpoint:. This study was used to establish the RfD. A 50% dermal absorption factor is required for this risk assessment because the dose identified is from an oral study.

This risk assessment IS required.

5. Inhalation Exposure (Any Time period).

Study Selected: NONE

MRID No.: Not Applicable

Executive Summary: Not Applicable

Dose/Endpoint for Risk Assessment: Not Applicable

Comments about Study/Endpoint: With the exception of an acute inhalation study, no inhalation studies are available for evaluation. Therefore, the HIARC has selected the oral NOAELs for inhalation risk assessment. Since an oral dose is used, risk assessment should follow the route-to-route extrapolation as below:

Step I. The inhalation exposure component (i.e. μ a.i./day) using 100% absorption rate (default value) and application rate should be converted to an **equivalent oral dose** (mg/kg/day)

Step II. The dermal exposure component (mg/kg/day) using a 50% dermal absorption rate and application rate should be converted to an **equivalent oral dose**. This dose should then be combined with the oral equivalent dose in Step I.

Step III. The combined oral equivalent dose from Step II should then be compared to the oral NOAELs to calculate the MOEs. The NOAELs are as follows:

For Short-Term:	6.3 mg/kg/day, from rabbit developmental toxicity. study, (MRID 41144703)
For Intermediate-/Long-Term	2.1 mg/kg/day, from 2-yr chronic rat study (MRID 40345607, 41147701)

NOTE: The inhalation and dermal components can be combined only for the long-term, since oral NOAELs were identified. They cannot be combined for short- or intermediate-term since dermal NOAELS were selected for these scenarios.

This risk assessment IS required.

D. Recommendation for Aggregate (Food, Water and Dermal) Exposure Risk Assessments

For glufosinate ammonium, route specific data are available for the oral and dermal exposure routes, but not the inhalation route. It is therefore necessary to convert any inhalation exposure to the oral equivalent, and calculate the MOE for use in the reciprocal MOE approach to calculating aggregate risk assessments. Appropriateness of this method is also established by the consistency of at least one endpoint, clinical signs of neurotoxicity, which is seen is both the oral and dermal studies.

E. Margins of Exposures for Occupational/Residential Exposure Risk Assessments

A MOE of 100 is adequate for occupational exposure. The MOE for residential exposure will be determined by the FQPA Safety Factor Committee.

III. CLASSIFICATION OF CARCINOGENIC POTENTIAL

1. Combined Chronic Toxicity/Carcinogenicity Study in Rats

MRID No. 40345607, 41144701

Discussion of Tumor Data There was no clear demonstration of increased tumor incidence following exposure to glufosinate ammonium.

Adequacy of the Dose Levels Tested Dosing levels were considered adequate in females based on mortality and inhibition on brain glutamine synthetase at 130 weeks; and adequate in males based on increased kidney weights and kidney/brain weights at 52 weeks.

2. Carcinogenicity Study in Rats

MRID No. 44539501

Discussion of Tumor Data Under the conditions of this study, there was no evidence of carcinogenic potential.

Adequacy of the Dose Levels Tested Dosing was considered adequate based on increased incidences of retinal atrophy.

3. Carcinogenicity Study in Mice

MRID No. 40345609, 41144702

Discussion of Tumor Data Under the conditions of this study, there was no evidence of carcinogenic potential in any treatment group..

Adequacy of the Dose Levels Tested Dosing was considered adequate based on increased mortality in males, increased glucose levels in males and females, and consistent changes in glutathione levels in males.

4. Additional Metabolism/Mechanistic Studies

None

5. Classification of Carcinogenic Potential based on the lack of mutagenic potential as assessed in a battery of mutagenicity assays, and the absence of treatment-related tumors in rats and mice at dose levels adequate for assessment, the HIARC has determined that glufosinate ammonium be classified as a **not likely** carcinogen.

IV. MUTAGENICITY

84-2 Unscheduled DNA Synthesis

Executive Summary: In an unscheduled DNA synthesis assay (MRID 40345614), primary rat hepatocyte cultures were exposed to HOE 039886 in deionized water at 15 concentrations ranging from 0.1 to 5240 µg/mL for 18 - 19 hours.

HOE 039866 was tested up to cytotoxic concentrations as evidenced by decreased survival rate as low as 34% **There was no evidence that unscheduled DNA synthesis was induced by the test material.**

This study is classified as **acceptahle.** It satisfies the requirement for FIFRA Test Guideline 84-2 for other genotoxic mutagenicity data.

84-2 DNA Damage/Repair in bacteria

Executive Summary: In a DNA damage/repair assay ()MRID 072962), glufosinate ammonium was exposed overnight to B. subtilis that lacks the capacity for repair (H45) at concentrations of 0, 50, 100, 500, 1000, 5000 or 10,000 µg/plate. Glufosinate ammonium was also exposed, at the same dose levels, to an isogenic sister strain which has the capacity for DNA repair (H17).

Under the conditions of the study, no difference in the inhibition of growth between these two strains was noted at any of the doses tested. Since the test measures the inhibition of growth in response to the test article, the requirement that chemicals be tested to the limits of cytotoxicity was satisfied. The positive controls, 2-(2-furyl)-3-(5-nitro-2-furyl)acrlamide (AF-2), caused a differential growth inhibition, whereas the negative controls (NaOH, HCL, and Kanamycin) produced no significant difference in growth inhibition. The test system was therefore sensitive to agents that damage DNA. **Under the conditions of the test, the test article failed to cause damage to DNA that could be detected by this repair assay.**

This study is classified as **acceptable**. It satisfies the requirement for FIFRA Test Guideline 84-2 for *in vitro* mutagenicity (DNA damage & repair) study..

84-2 Gene mutation assay in Salmonella typhimurium strains

Executive Summary: In a bacterial cell gene reverse mutation assay (MRID 072962) Salmonella typhimurium strains TA98, TA100, TA1535 and TA1537 were exposed to glufosinate ammonium (92.1% a.i.) at concentrations of 0, 5, 10, 50, 100, 500, and 1000 µg/plate in the presence and absence of mammalian metabolic activation (S9-mix).

No increases in mutation frequencies, with or without metabolic activation, were noted in any of the test strains at any of the doses tested. Virtually total inhibition of growth was noted in all strains at the highest dose, 1000 µg/plate. Therefore, the requirement that chemicals be tested to the limits of cytotoxicity was satisfied. The positive controls, 2-aminoanthracene, AF-2, 1-ethyl-2-nitro-3-nitroso-guanidine, 9-amino-acridine, and 2-nitro-fluorine, induced the appropriate responses. Therefore the test systems were sensitive to agents that induce gene mutation. Under the conditions of the test, glufosinate- ammonium failed to cause reverse mutations in bacteria with and without metabolic activation

This study is classified as **acceptable**. It satisfies the requirement for FIFRA Test Guideline 84-2 for in vitro mutagenicity (bacteria reverse gene mutation) data.

84-2 Mouse Lymphoma Forward Mutation Assay

Executive Summary: In a mouse lymphoma L5179Y forward mutation assay(MRID 40345616.), HOE 039866 was tested at seven nonactivated doses of 50 to 5000 μg/mL or at six S9-activated doses of 300 to 5000 μg/mL.

HOE 39866 did not increase the mutation frequency at the thymidine kinase locus. The solvent controls gave acceptable values and the positive controls ethylmethanesulfonate (nonactivated) and 3-methylcholanthrene (S9-activated) provided evidence that the assay had adequate sensitivity for detecting mutagenicity.

This study is classified as **acceptable**. It satisfies the requirement for FIFRA Test Guideline 84-2 for in vitro mutagenicity (mouse lymphoma forward mutation) data.

84-2 Mouse Micronucleus Assay

Executive Summary: In a mouse micronucleus assay (MRID 41144704.) 13 groups of mice (5/sex/dose) received a single administration of HOE 039866 at dose levels of 100, 200, and 350 mg/kg by gavage. A positive control group received 50 mg/kg of cyclophosphamide. After dosing, the animals were sacrificed at 24, 48, and 72 hrs., and the erythrocytes from the bone marrows were sampled at these times. The results indicated the test agent had no effect on micronucleus formation. This observation was consistent with that of a previous in vivo micronucleus assay (HED Document Nos. 004403, 004928, 006936).

This study is classified as **acceptable**. It satisfies the requirement for FIFRA Test Guideline 84-2 for in vivo mutagenicity (mouse micronucleus) data.

CONCLUSION. The HIARC concluded that **"there was no evidence to suggest that the test material, glufosinate ammonium, was mutagenic under the testing conditions."**

V. FQPA CONSIDERATIONS

1. ***Neurotoxicity***

■ An acute delayed neurotoxicity study in the hen was not available. An acute neurotoxicity study (§81-7) was not available.

■ A subchronic neurotoxicity study (§82-5) was available, and while not satisfying the guideline requirements, suggested that glufosinate ammonium has significant neurotoxicity potential based on increases in the incidence of decreased exploratory activity, decreased alertness, decreased startle response and meiosis at 521 mg/kg/day and above.

Evidence of Neurotoxicity from Other Data

■ In a developmental toxicity study in rats (MRID 40345610, 073916, 072965), hyperactivity was observed in dams at 50 mg/kg/day and above.

■ In a 21-day dermal study in rats (MRID 40645605) aggressive behavior, piloerection and a high startle response were observed at 300 mg/kg/day and above.

■ In a 2-year carcinogenicity study in rats (MRID 43864246, 44539501) retinal atrophy was observed at 228.9 mg/kg/day and above

2. **Developmental Toxicity**

■ there is no evidence of increased susceptibility of rat or rabbit fetuses to *in utero* exposure in developmental studies

■ a developmental neurotoxicity study in rats was not available.

3. **Reproductive Toxicity**

■ in the two generation reproduction study effects in the offspring were observed only at or above treatment levels which resulted in parental toxicity.

4. **Additional information from the literature**

No relevant citations were found.

5. **Determination of Susceptibility**

■ The data provided **no indication of increased sensitivity** in rats or rabbits to pre- and/or postnatal exposure to glufosinate ammonium.
■ In the developmental toxicity study in rats the fetal NOAEL/LOAEL was 50 /250 mg/kg/day based on dilated renal pelvis and/or hydroureter. These levels were higher than the maternal NOAEL/LOAEL which was 10 / 50 mg/kg/day based on vaginal bleeding and hyperactivity.
■ In the rabbit developmental toxicity study the NOAEL for both maternal toxicity was 2.0 mg/kg/day. The LOAEL is 6.3 mg/kg/day based on reduced food consumption, body weight and weight gains and increased kidney weights. In fetuses, the NOAEL was 6.3 mg/kg/day based on decreased fetal body weight and increased fetal death at 20 mg/kg/day.
■ In the two-generation reproduction study, the LOAEL for systemic toxicity is 120 ppm (6 mg/kg/day) based on increased kidney weights in both sexes and generations. The systemic toxicity NOAEL is 40 ppm (2 mg/kg/day). The LOAEL for reproductive/developmental toxicity is 360 ppm (18 mg/kg/day) based on decreased number of viable pups in all generations. The NOAEL is 120 ppm (6 mg/kg/day).

6. **Recommendation for a Developmental Neurotoxicity Study**

(i) Evidence supporting a developmental neurotoxicity study

■ Evidence of neurotoxicity in the unacceptable subchronic neurotoxicity study
■ Evidence of neurotoxicity in the 21-day dermal study.
■ Evidence of neurotoxicity in dams in the rat developmental toxicity study.
■ Evidence of neurotoxicity in chronic and/or carcinogenicity studies in the rat, mouse and dog.
■ Lack of acceptable acute and subchronic neurotoxicity studies.

(ii) Evidence that does not support a developmental neurotoxicity study

■ No evidence of neurotoxicity in rat offspring in the rat multigeneration reproduction study at levels that caused a decrease in the number of viable pups.
■ Susceptibility not demonstrated in developmental or reproductive studies.

Based on the demonstration of neurotoxicity in several studies, and the absence of critical studies, the HIARC has determined that **data gaps exist for acute neurotoxicity, subchronic neurotoxicity and developmental neurotoxicity**.

7. **Determination of the FQPA Safety Factor**

The application of and FQPA factor for the protection of infants and children from exposure to glufosinate ammonium, as required by FQPA, will be determined during risk characterization.

VI. HAZARD CHARACTERIZATION

Glufosinate ammonium (also referred to as DL-glufosinate ammonium or HOE 039866) is toxicity category III for acute oral, dermal and inhalation toxicities. It is toxicity category II for eye irritation. It is not a dermal irritant nor is it a dermal sensitizer. For subchronic toxicity, the primary effects in the mouse were increased liver and kidney weights with increases in serum aspartate amino transferase and alkaline phosphatase. Signs of neurotoxicity were observed in rats in subchronic studies, such as aggressive behavior, piloerection, high startle response, increased incidence of fearfulness.

In the chronic studies in the rat, increased mortality, increased occurrence of retinal atrophy, and inhibition of brain glutamine synthetase were observed, as were increased liver and kidney weights. In the mouse, increase mortality was observed, as was changes in glucose levels consistent with changes in glutathione levels. Increased mortality and EKG alterations were observed in dogs. **There was no evidence of a treatment-related increase in tumors.**

The developmental toxicity study in the rat produced dilated renal pelvis and/or hydroureter in the offspring at levels that produced significant increases in hyperactivity and vaginal bleeding in dams. In the rabbit, decreased fetal body weight and increased mortality were observed at 20 mg/kg/day, while in rabbit dams, decreased food consumption, body weight and body weight gain were observed at 6.3 mg/kg/day.

The reproductive toxicity study indicated systemic and postnatal developmental toxicity at 6.0 mg/kg/day in the form of increased kidney weights in parents, and a decrease in viable pups in all generations. Since parental and developmental effects were observed at the same dose levels, **there is no evidence of increased susceptibility in offspring.**

A **consistent pattern of neurotoxicity was seen** in several studies, including the subchronic, developmental and chronic studies in rats, mice and dogs. In addition to the clinical signs such as hyperactivity, aggressive behavior, piloerection, high startle response, retinal atrophy was observed. Changes in glutamine synthetase levels were observed in liver, kidney and brain in rats. These occurrences raise concern for the mechanism of neurotoxicity in these studies, an area where there are data gaps. It is expected that the requested neurotoxicity studies (see Data Gaps section) will provide the information needed for further characterization of these effects.

There is no concern for mutagenic activity in several studies including: Salmonella E. Coli, *in vitro* mammalian cell gene mutation assays, mammalian cell chromosome aberration assays, *in vivo* mouse bone marrow micronucleus assays, and unscheduled DNA synthesis assays.

A rat metabolism study with dermal application indicated that about 50% of the given radioactivity was absorbed 48 hours after a single dose application. In other metabolism studies, it was shown that over 80% of administered radioactivity is excreted within 24 to 48 hours as the parent compound in the feces and kidneys. Highest tissue levels were found in liver, kidney and gonads.

Additional testing was conducted in the major metabolites, known as HOE 061517 and HOE 099730, as well as the L-isomer, known as HOE 058192. These compounds, tested in subchronic rat, mouse and dog studies, and in developmental toxicity studies in rat and rabbit. showed a similar profile of toxicity as the parent compound (HOE 039866).

VII. DATA GAPS

Three data gaps have been identified at this time: acute neurotoxicity, subchronic neurotoxicity and developmental neurotoxicity. These studies are to be requested because of concern for the neurotoxic effects observed in several studies and multiple species. It is also requested that glutamine synthetase levels be measured in the subchronic neurotoxicity study to assist the Agency in characterizing these effects.

VIII. ACUTE TOXICITY

ACUTE TOXICITY for Glufosinate ammonium Technical

STUDY TYPE	RESULTS	Toxicity Category
81-1 acute oral–rat MRID 41796102	LD_{50} 4010 mg/kg in males LD_{50} 3030 mg/kg in females	III
81-2 acute dermal MRID 41796103	LD_{50} > 2000 mg/kg in males & females	III
81-3 acute inhalation MRID 41846302	LC_{50} 4.42 mg/L estimated in males & females	III
81-4 eye irritation MRID 417+6104	eye irritant; comeal opacity reversible within 14 days	II
81-5 dermal irritation MRID 41796105	not a dermal irritant	IV
81-6 sensitization MRID 41796106	not a dermal sensitizer	NA

IX SUMMARY OF TOXICOLOGY ENDPOINT SELECTION

The doses and toxicological endpoints selected for various exposure scenarios are summarized below.

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	6.3	LOAEL = 20 mg/kg/day based on decreased fetal body weight and increased fetal death	developmental toxicity–rabbit
	Acute RfD = 0.06 mg/kg (females 13+only) Acute RfD None for general population including infants and children		
Chronic Dietary	NOAEL = 2.1 UF = 100	LOAEL = 6.8 / 8.2 m mg/kg/day in males / females based on increased kidney weight and kidney/brain weight in males at 52 weeks, and decreased survival in females at 130 weeks.	Two-year chronic toxicity/oncogenicity in rat
		Chronic RfD = 0.02 mg/kg day	
Short-Term (Dermal)	100	LOAEL = 300 mg/kg/day based on clinical observations (aggressive behavior, piloerection & high startle response)	21-day dermal–rat
Intermediate-Term (Dermal)	100	LOAEL = 300 mg/kg/day based on clinical observations (aggressive behavior, piloerection & high startle response)	21-day dermal–rat
Long-Term (Dermal)	NOAEL = 2.1 UF = 100	LOAEL = 6.8 / 8.2 m mg/kg/day **oral** in males / females based on increased kidney weight and kidney/brain weight in males at 52 weeks, and decreased survival in females at 130 weeks. **50% dermal absorption demonstrated.**	Two-year chronic oral toxicity/oncogenicity in rat
Short Term (Inhalation)	2	LOAEL = 6.3 mg/kg/day based on decreased body weight, body weight gain, food consumption, increased kidney weights in dams	developmental toxicity–rabbit
Intermediate Term (Inhalation)	2.1	LOAEL = 6.8 / 8.2 m mg/kg/day **oral** in males / females based on increased kidney weight and kidney/brain weight in males at 52 weeks, and decreased survival in females at 130 weeks.	Two-year chronic oral toxicity/oncogenicity in rat
Long Term (Inhalation)	2.1	LOAEL = 6.8 / 8.2 m mg/kg/day **oral** in males / females based on increased kidney weight and kidney/brain weight in males at 52 weeks, and decreased survival in females at 130 weeks.	Two-year chronic oral toxicity/oncogenicity in rat

013728

Attachment 2: Report of the FQPA SafetyFactor Committee. 17-MAY-1999

HED Doc. No. 013373, B. Tarplee, 17-May-1999

HED DOC. NO. 013373

17-MAY-1999

MEMORANDUM

SUBJECT: ***GLUFOSINATE AMMONIUM*** - Report of the FQPA Safety Factor Committee.

FROM: Brenda Tarplee, Executive Secretary
FQPA Safety Factor Committee
Health Effects Division (7509C)

THROUGH: Ed Zager, Chair
FQPA Safety Factor Committee
Health Effects Division (7509C)

TO: Melba Morrow, Branch Senior Scientist
Registration Branch 1
Health Effects Division (7509C)

PC Code: 128850

The Health Effects Division (HED) FQPA Safety Factor Committee met on May 10, 1999 to evaluate the hazard and exposure data for glufosinate ammonium and recommended that the FQPA Safety Factor (as required by the Food Quality Protection Act of August 3, 1996) be reduced to 3x in assessing the risk posed by this chemical.

I. HAZARD ASSESSMENT

1. Adequacy of Toxicity Database

There are no datagaps for the assessment of the effects of glufosinate ammonium following *in utero* and/or postnatal exposure. However, based on the toxicity profile, acute and subchronic neurotoxicity and developmental neurotoxicity studies in rats are required.

The HIARC determined that a developmental neurotoxicity study in rats is **required** because a consistent pattern of neurotoxicity was seen in several studies, including the subchronic, developmental and chronic studies in rats, mice and dogs. In addition to the clinical signs such as hyperactivity, aggressive behavior, piloerection, high startle response, retinal atrophy was observed. Changes in glutamine synthetase levels were observed in liver, kidney and brain in rats. These occurrences raise concern for the mechanism of neurotoxicity in these studies, an area where there are data gaps. It is expected that the requested neurotoxicity studies will provide the information needed for further characterization of these effects (DRAFT Report of the HIARC; M. Ottley to M. Morrow dated May 17, 1999).

2. Determination of Susceptibility

The HIARC (meeting date May 5, 1999) concluded that the data provided no indication, either quantitatively or qualitatively, of increased susceptibility in rats or rabbits, to pre- and/or postnatal exposure to glufosinate ammonium. In the prenatal developmental toxicity studies in rats and rabbits and the two-generation reproduction study in rats, any observed toxicity to the fetuses or offspring occurred at equivalent or higher doses than did toxicity to parental animals (*Memorandum*: M. Ottley, RAB1, to the FQPA SFC, dated May 6, 1999).

II. EXPOSURE ASSESSMENT AND RISK CHARACTERIZATION

1. Dietary (Food) Exposure Considerations

Glufosinate ammonium is currently registered for use on foods considered to be highly consumed by infants and children (including apples, grains, and milk). All established tolerances, however, are time-limited due to the lack of a rat carcinogenicity study (this study has recently been submitted to the Agency).

In *non-transgenic crops*, the tolerance expression includes glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid. Glufosinate ammonium is registered for use on apples, grapes, bananas and the tree nut group resulting in tolerances ranging from 0.05 - 0.3 ppm. Tolerances are also established for these two compounds as a result of secondary residues in eggs and milk, and fat, meat and meat byproducts of cattle, goats, hogs, poultry and sheep ranging from 0.05 ppm - 0.3 ppm.

In *transgenic crops*, the tolerance expression includes glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate. Glufosinate ammonium is registered for use on transgenic corn and soybeans and a Section 18 is established for use on transgenic sweet corn in Wisconsin. Tolerances range from 0.2 ppm to 6.0 ppm and in aspirated grain fractions at 25 ppm. Codex MRLs are established or proposed on almond hulls, pome fruit, tree nuts, bananas, potatoes, maize (and forage), soy beans, and sugar beets.

There are no monitoring data available for glufosinate ammonium, however, adequate field trial data have been submitted and indicate the presence of quantifiable residues. Percent crop treated (%CT) data have also been provided to HED by BEAD for apples, corn, and soybeans.

The previous dietary exposure analyses using the Dietary Exposure Evaluation Model (DEEM) included tolerance level residues and 100% CT for all commodities, resulting in an overestimate of dietary exposure. However, if needed, the DEEM analyses could be refined to include anticipated residues calculated from field trial data and %CT data. Even if these refinements are made, the dietary exposure estimates are still expected to be protective.

2. Drinking Water Exposure Considerations

The environmental fate data for the parent, glufosinate ammonium, are adequate to characterize drinking water exposure. These data indicate that the parent compound is mobile and persistent and therefore, it is likely to move to groundwater and to persist in groundwater and surface water. Additional environmental fate data is needed for the degradates.

Targeted monitoring data are not currently available. Tier I Estimated Environmental Concentrations (EECs) for glufosinate-ammonium were calculated using the GENEEC (surface water) and SCI GROW (groundwater) screening level models based on information from the Rely® label.

3. Residential Exposure Considerations

Glufosinate ammonium is the active ingredient in registered residential products formulated as a non-selective post-emergence herbicide for use as spot treatments around trees, shrubs, fences, walks, patios, driveways, sidewalks, in flower beds, around houses, buildings, wooded lots, storage and recreational areas. These products can also be used

for lawn renovation at an application rate of 1.45 lb ai/Acre. Repeat treatments are allowed to control plants generating from underground parts or seed.
No chemical-specific data are available, therefore, the *Draft Standard Operating Procedures for Residential Exposure Assessments* will be used to estimate the potential post-application exposure to infants and children resulting from the use of products containing glufosinate ammonium. A dermal absorption rate of 50% (from a pharmacokinetic study in rats) will also be used in these assessments.

Several reports of adverse reactions in humans concerning products containing glufosinate ammonium active ingredient were cited in the incidents section of the REFS database (30-NOV-1998). All of the incidents in humans are described as of "unknown certainty" with mostly minor or unrelated effects.

III. SAFETY FACTOR RECOMMENDATION AND RATIONALE

1. FQPA Safety Factor Recommendation

The Committee recommended that the **FQPA safety factor** for protection of infants and children (as required by FQPA) be **reduced to 3x.**

2. Rationale for Requiring the FQPA Safety Factor

The FQPA SFC concluded that a safety factor is required for glufosinate ammonium since there is uncertainty due to the data gaps for the acute and subchronic neurotoxicity studies in rats and the developmental neurotoxicity study in rats which has been required by the HIARC.

The Committee recommended that the **FQPA safety factor** be **reduced** to 3x because:

- there is no quantitative or qualitative indication of increased susceptibility in the prenatal developmental toxicity studies in rats and rabbits or in the two-generation reproduction study in rats with the parent compound, the isomer, or metabolites of concern;
- adequate data are available or conservative modeling assumptions are used to assess the potential for dietary (food and drinking water) and residential exposure to infants and children.

Additionally, the Committee recommended that the weight-of-evidence for the FQPA safety factor recommendation be re-evaluated after all data requirements for glufosinate ammonium have been satisfied.

3. Application of the Safety Factor - Population Subgroups

The FQPA safety factor for glufosinate ammonium is **applicable to all population subgroups** since there is uncertainty due to the data gaps for the acute and subchronic neurotoxicity studies in rats and the developmental neurotoxicity study in rats which has been required by the HIARC.

4. Application of the Safety Factor - Risk Assessment Scenarios

The FQPA safety factor for glufosinate ammonium is **applicable to all risk assessments** (acute/chronic dietary and residential scenarios) since there is uncertainty due to the data gaps for the acute and subchronic neurotoxicity studies in rats and the developmental neurotoxicity study in rats which has been required by the HIARC.

013729

Attachment 3: Evaluation of Residue Data and Analytical Methods

D257629 & D257628, T. Bloem, 9-July-1999

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

9-July-1999

MEMORANDUM

Subject: PP#s 7F04910, 8F04997 - AgrEvo USA Company has Requested a Section 3 Registration for use of Glufosinate Ammonium (Liberty™ and Rely®) on Potatoes, Transgenic Sugar Beets and Transgenic Canola. **Evaluation of Residue Data and Analytical Methods.** DP Barcodes D257629, D257628. Chemical # 128850. Case #s 289177, 290273. Submission #s S529287, S545114

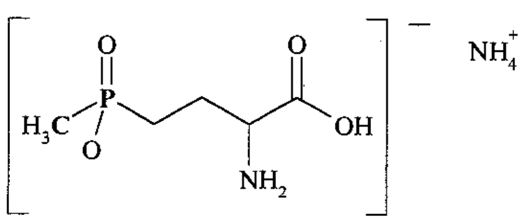
From: Tom Bloem, Chemist
RAB1/HED (7509C)

Through: Melba Morrow, DVM, Branch Senior Scientist
George Kramer, Ph.D., Chemist
RAB1/HED (7509C)

To: Joanne Miller/Eugene Wilson (PM Team 23)
RD (7505C)

AgrEvo USA Company has requested a Section 3 registration for use of glufosinate ammonium on potatoes, transgenic sugar beets and transgenic canola. Review of the metabolism studies were initially conducted by Dynamac. The Dynamac review has undergone secondary review by RAB1 and has been revised to reflect current division policies.

glufosinate ammonium (ammonium-DL-homoalanin-4-yl(methyl) phosphinate)



BACKGROUND

Glufosinate-ammonium is a racemic mixture of the D- and L-isomers; only the L-isomer is herbicidally active. The compound is a non-selective herbicide and acts as a inhibitor of glutamine synthetase which leads to poisoning of the plant by ammonia. Glufosinate-ammonium is currently registered for use on both transgenic and non-transgenic crops. Transgenic plants contain a gene (phosphiothrion-acetyl-transferase) which enables the plant to metabolize the herbicidally active moiety of glufosinate-ammonium into a N-acetyl glufosinate (2-acetamido-4-methylphosphinico-butanoic acid; which is not herbicidally active). This metabolite is found only in transgenic plants. The petitioner is proposing the establishment of permanent tolerances for the combined residues of glufosinate ammonium and its metabolites 2-acetamido-4-methylphosphinico butanoic acid and 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents in/on the following commodities:

Beet, sugar, root	0.7 ppm
Beet, sugar, tops (leaves)	1.3 ppm
Beet, sugar, molasses	5.0 ppm
Canola, seed	0.4 ppm
Canola, meal	2.0 ppm
*Potato	0.4 ppm
*Potato, processed	1.0 ppm
*Potato, flakes	1.3 ppm

** tolerance for combined residues of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid (non-transgenic crop)*

Time-limited tolerances, with an expiration date of July 13, 1999, have been established for residues of glufosinate-ammonium and its metabolite, 3-methylphosphinico propionic acid, in/on almond hulls, apples, grapes, the tree nuts group, eggs, milk, and the fat, meat, and meat byproducts of ruminants and poultry [40 CFR §180.473(a)]. An import tolerance with an expiration date of January 18, 2000 has been established for combined residues of glufosinate-ammonium and its metabolite, 3-methylphosphinico propionic acid, expressed as glufosinate acid equivalents, in/on bananas [40 CFR §180.473(b)]. Time-limited tolerances, with an expiration date of July 13, 1999, have been established for residues of glufosinate-ammonium and its metabolites, 2-acetamido-4-methylphosphinico-butanoic acid and 3-methylphosphinico propionic acid, in/on aspirated grain fractions, field corn grain, forage, and stover, soybeans, and soybean hulls derived from transgenic field corn and transgenic soybeans [40 CFR §180.473(c)]. A Section 18 request from Wisconsin for use of glufosinate ammonium on transgenic sweet corn has been approved (4.0 ppm tolerance established for residues of glufosinate-ammonium and its metabolites, 2-acetamido-4-methylphosphinico-butanoic acid and 3-methylphosphinico propionic acid expressed as glufosinate acid equivalents). Tolerances were established on a time-limited basis due to a lack of a carcinogenicity study.

The following terms are used interchangeably throughout this document:

glufosinate ammonium = HOE 039866
N-acetyl glufosinate = 2-acetamido-4-methylphosphinico-butanoic acid, HOE 099730, HOE 085355
3-methylphosphinico propionic acid = HOE 061517, MP-propionic acid

EXECUTIVE SUMMARY OF CHEMISTRY DEFIC.ENCIES

- Revised Section B (Liberty™ and Rely®)
- Revised Section F (transgenic canola, transgenic sugar beet and potato)
- Storage Stability for Sugar Beet Processed Commodities (3 months)
- Analytical Chemistry Branch Validation of Proposed Tolerance Enforcement Methods
- Description of GC/MS Confirmatory Method

CONCLUSIONS

OPPTS GLN 830 Series: Product Properties

1. Product chemistry data for glufosinate ammonium has been submitted, reviewed and found acceptable. No additional product chemistry data is necessary for this petition (PP#8F3607, J. Garbus, 14-Oct-1988 and 8-Aug-1990).

OPPTS GLN 860.1200: Directions for Use

2a. The sugar beet portion of the Liberty™ Herbicide label should be amended to indicate in the "Special Notes" section that the maximum single application rate is 42 fluid ounces/acre (0.48 lbs ai/acre).

2b. The maximum seasonal application rate for canola is listed as 0.77 lbs ai/acre in the application timing section and 0.73 lbs ai/acre in the special notes section (0.77 lbs ai/acre will be assumed to be correct). The petitioner indicated that only the spring variety of canola has been genetically modified for tolerance to glufosinate ammonium. In Region 2, canola is only planted in the winter months (winter variety of canola) due to the unfavorable climate for canola in the summer. Therefore, the petitioner is not requesting registration of transgenic canola in Region 2. The canola portion of the Liberty™ Herbicide label should be amended to indicate in the "Special Notes" section that use of this product on transgenic canola in Region 2 is prohibited.

2c. Both the Rely® Herbicide and Liberty™ Herbicide labels should be amended to indicate a 120 day plant back interval for all crops except wheat where a 70 day plant back interval is appropriate.

OPPTS GLN 860.1300: Nature of the Residue - Plants

3a. ***Sugar Beet:*** The qualitative nature of glufosinate ammonium residues in transgenic sugar beets is adequately understood. Total radioactive residues (TRR) were 2.05 ppm in tops and 0.93 ppm in roots harvested 146 days following the last of 2 applications of [C^{14}]glufosinate-ammonium at 0.54 lbs ai/acre (total application rate 1.07 lbs ai/acre, 1.1x the maximum proposed single and seasonal application rates). Samples of sugar beet commodities were also collected at shorter preharvest intervals (PHIs); TRR were 20.08 ppm in tops and 2.01 ppm in roots collected 1 hour after the second application and were 12.26 ppm in tops and 6.75 ppm in roots collected 21 days after the second application.

In sugar beet tops and roots (all PHIs), 93-98% of the TRR was identified. The N-acetyl glufosinate metabolite was the major residue in all sugar beet top and root samples (55.2-67.9% TRR), except 0-day PHI tops where glufosinate ammonium accounted for 84.6% of the TRR (N-acetyl glufosinate accounted for 13.4% of the TRR). Glufosinate-ammonium accounted for 19.1-41.8% of the TRR in all other sugar beet top and root samples. 3-Methylphosphinico propionic acid was identified at low levels in all sugar beet samples (0.4-6.0% TRR). One additional metabolite, 2-methylphosphinico acetic acid, was identified in 146 day PHI tops at 0.07% TRR.

The current tolerance expression for commodities derived from transgenic crops includes the major residues identified in the sugar beet metabolism study and is adequate for commodities derived from transgenic sugar beet. The residues of concern in/on transgenic sugar beets are glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate.

3b. ***Canola:*** Total radioactive residues (TRR) were 0.021-0.064 ppm in foliage, 0.134-0.220 ppm in roots, 0.076-0.263 ppm in hulls, and 0.045-0.109 ppm in seed harvested 120 days (at maturity) following a single application of [^{14}C]glufosinate-ammonium at 0.67 lbs ai/acre (0.9x the maximum proposed seasonal rate). Samples of canola commodities were also collected at shorter PHIs; TRR were 144.578 ppm in the entire plant collected at 1-hour PHI, and were 3.207 and 5.343 ppm in foliage, and 3.807 and 5.192 ppm in roots collected at 21-day PHI.

In the whole plant harvested 1 hour posttreatment, the parent accounted for the majority of the radioactivity (72.9% TRR, 105.4 ppm); N-acetyl-glufosinate was identified at 18.2% of the TRR (26.3 ppm). In foliage harvested 21 days posttreatment, the major residue was N-acetyl-glufosinate (60.2% TRR, 3.22 ppm); the parent was present at 20.7% of the TRR (1.11 ppm) and a small amount of 3-methylphosphinico propionic acid was identified (6.7% TRR, 0.358 ppm).

In mature canola seed and hulls (0.109 ppm and 0.263 ppm, respectively), 40-58% of the TRR was identified (the remainder of the extracted radioactivity was described as unknown metabolites equivalent to the LOD). Glufosinate-ammonium and 3-methylphosphinico propionic acid were the major residues identified, accounting for 5.0-44.8% of the TRR (0.007-0.118 ppm). The N-acetyl-glufosinate metabolite was a minor residue accounting for 1.1-13.9% of the TRR (0.001-0.037 ppm). In canola seed, radioactive residues associated with water-soluble polysaccharides and/or proteins accounted for 12.4% of the TRR (0.014 ppm).

The submitted study is marginally adequate to describe the nature of the residue in glufosinate tolerant canola. The test substance was applied at less than 1x the maximum proposed seasonal rate which resulted in low levels of radioactivity in canola seed, making identification of residues difficult. The storage interval prior to analysis and extraction of whole plant and canola foliage (19 months) were not within the validated time interval (12 months). Seed and hull samples were analyzed using HPLC systems 1 and 2 (whole plant and foliage samples analyzed by system 1 only). Different levels of parent, N-acetyl glufosinate and 3-methylphosphinico propionic acid were observed depending on which system was used. No explanation for this difference was provided. Since adequate metabolism studies on the transgenic varieties of field corn and soybeans have been previously submitted (D211531 and D219069, M. Rodriguez, 7-Mar-1996) and the results from the canola study do not significantly differ from these studies, no additional data pertaining to the metabolism of glufosinate-ammonium in transgenic canola are required. The residues of concern in/on transgenic canola are glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate.

3c. ***Potato:*** The nature of the residue is considered to be understood in genetically unaltered lettuce, soybeans, corn, apples and wheat. After application of ^{14}C glufosinate ammonium to the nutrient medium (water or soil) in which these crops were grown, only one labeled metabolite could be identified, 3-methylphosphinico propionic acid (parent was not found). HED concluded that the residues to be regulated in commodities derived from genetically unaltered lettuce, soybeans, corn, apples and wheat are glufosinate ammonium and 3-methylphosphinico propionic acid (PP#8F3607, J. Garbus, 8-Aug-1990).

A metabolism study has not been performed on a root vegetable (potato). Since the metabolism of glufosinate ammonium is consistent in four diverse crops groups (lettuce [leafy vegetable], soybeans [legume vegetable], wheat [cereal grain] and apple [fruit]) the nature of glufosinate ammonium residues in potatoes will be considered to be understood. The residues of concern in/on potatoes are glufosinate ammonium and 3-methylphosphinico propionic acid.

OPPTS GLN 860.1300: Nature of the Residue - Animals

4. The nature of glufosinate ammonium residues in lactating goats and hens is considered to be understood. It was shown that glufosinate ammonium and its metabolite (3-methylphosphinico propionic acid) are largely excreted and do not accumulate too any great degree in animal tissues. The only identifiable compounds in feces, urine, milk, eggs and tissues were the parent and 3-methylphosphinico propionic acid. HED concluded that the residues of concern in commodities derived from ruminants and poultry are glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid (PP#8F3607, J. Garbus, 8-Aug-1990).

   Transgenic field corn, soybeans, canola and sugar beets contain a second metabolite, N-acetyl glufosinate, which may lead to secondary residues of this compound in animal commodities. Feeding studies conducted on dairy cows and laying hens were submitted and reviewed as part of glufosinate ammonium registration on transgenic field corn and soybeans. In these studies, dairy cows and hens were feed a diet consisting of glufosinate ammonium and N-acetyl glufosinate. It was determined, that the tolerance expression for poultry (new tolerance as a result of registration on transgenic soybeans and transgenic field corn) should include glufosinate ammonium and 3-methylphosphinico propionic acid (N-acetyl glufosinate should not be included; D232571, M. Rodriguez). Additionally, it was determined that the currently established egg, milk, and fat, meat, and meat byproducts tolerances on cattle, goats, hogs, horses, poultry, and sheep were adequate (D211531 and D219069, M. Rodriguez, 7-Mar-1996).

OPPTS GLN 860.1340: Residue Analytical Method

5a. Analytical methodology is available in PAM II for determination of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid in genetically unaltered apples, bananas, grapes and tree nuts (HRAV-5A) and in milk, eggs and the tissues of ruminants and poultry (HRAV-12, also called BK/01/95). Method HRAV-5A employs extraction of glufosinate ammonia and its metabolite 3-methylphosphinico propionic acid from a 25 gram homogenized sample with water. The aqueous extract is filtered and subjected to anion-exchange chromatography for removal of interfering compounds. The residues are eluted from the resin with formic acid and derivatized by refluxing with trimethylorthoacetate. The derivatized residues are cleaned up on a silica gel column and quantified by GC/FPD. Concentrations are expressed in terms of glufosinate free acid equivalents. Method HRAV-12 (used to determine residue levels in animal matrices) is similar to the plant method except for an addition step. Water extracts of tissues are diluted with acetone to precipitate protein, centrifuged and then subjected to anion ion-exchange chromatography.

5b. In transgenic crops a second metabolite, N-acetyl glufosinate, is present. Since glufosinate ammonium and N-acetyl glufosinate are derivatized to the same compound, HRAV-5A does not distinguish between these two compounds. A second method, AE-24, was developed for individual determination of the three compounds regulated in commodities derived from transgenic crops. Method AE-24 is a modification of HRAV-5A in that following anion exchange, cation exchange is performed. Two fractions are collected from the cation ion exchange column. One fraction contains N-acetyl glufosinate and MP propionic acid and the second fraction contains glufosinate ammonium. Each fraction is derivatized by refluxing with trimethylorthoacetate, cleaned up on a silica gel column and quantified by GC/FPD. All compounds are quantified in terms of glufosinate free acid equivalents.

5c. Several variations of these two methods were used for quantitation of residues in the submitted field trials; all of which are adequate for data gathering purposes. Two of these methods, BK/04/95 (used for quantitation of residues in/on transgenic sugar beet commodities) and HRAV-24 (used for quantitation of residues in/on transgenic canola commodities), were submitted to the Analytical

Chemistry Branch (ACB) for Petition Method Validation (D254830, T. Bloem, 1-Apr-1999). Method BK/04/95 is similar to the current analytical enforcement method HRAV-5A but with modifications for application to a root crop. Method HRAV-24, which employs the cation exchange fractionation procedure (cation exchange procedure has not undergone Agency validation), was submitted to ACB for validation.

5d. Given that the registrant has provided concurrent fortification data to demonstrate that BK/04/95 and HRAV-24 are adequate for data collection purposes and these methods are a modification of the current tolerance enforcement method, HED concludes that they are suitable enforcement methods to support tolerances associated with a conditional registration on potatoes, transgenic sugar beets and transgenic canola. As a condition of the registration, HED will require a successful petition method validation and the registrant will be required to make any necessary modifications to the method resulting from petition method validation. Additionally, a complete description of the GC/MS confirmatory technique should be submitted by the petitioner.

OPPTS GLN 860.1360: Multiresidue Method

6. Glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate were not quantitatively recovered from any of the FDA Multiresidue Testing Protocols. This information has been forwarded to FDA (PP#8F3607, J. Garbus, 14-Aug-1988; PP#5F4578, M. Rodriguez, 10-Oct-1995).

OPPTS GLN 860.1380: Storage Stability Data

7. The submitted storage stability study indicates that glufosiante ammonium, N-acetyl glufosinate and 3-methylphosphinico propionic acid are stable in transgenic sugar beet tops and roots for 24 months.

   Previously submitted and reviewed storage stability data indicate that glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid are stable for 24 months in apples, corn grain and soybeans (PP#8F3607, J. Garbus, 8-Aug-1990). Additional storage stability data indicate that glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate are stable for 12 months in transgenic soybean seed, forage and hay; for 3 months in soybean oil and meal; for 6 months in transgenic corn grain, fodder and forage; and for 3 months in eggs, liver, kidney and muscle (D211531 and D219069, M. Rodriguez, 7-Mar-1996).

OPPTS GLN 860.1480: Meat/Milk/Poultry/Eggs

8. Two dairy cow and two poultry feeding studies have been previously submitted, reviewed and determined to be adequate: **(1)** dairy cows and poultry feed a diet containing a 3:1 mixture of glufosinate ammonium and 3-methylphosphinico propionic acid (PP#8F3607, J. Garbus, 8-Aug-1990) and **(2)** dairy cows and poultry feed a diet containing 15% glufosinate ammonium and 85% N-acetyl glufosinate (D211531 & D211531, M. Rodriguez, 7-Mar-1996). Two feeding studies were performed on dairy cows and poultry due the different residues present in transgenic (principally N-acetyl glufosinate followed by glufosinate ammonium) and non-transgenic crops (principally 3-methylphosphinico propionic acid). Since the majority of the dietary burden to ruminants and poultry originates from transgenic crops, the feeding studies performed with N-acetyl glufosinate and glufosinate ammonium will be considered representative.

   Considering all registered and proposed crops the maximum theoretical dietary burden is 14.55 ppm for beef cattle (aspirated grain fractions, corn field forage, cannery waste), 14.22 ppm for dairy cattle (aspirated grain fractions, corn field forage, cannery waste, molasses), 2.62 ppm for poultry (soybean hulls, soybean meal, soybean seed, canola meal) and 8.07 ppm for swine (aspirated grain fractions, canola meal, potato culls). Using these dietary burdens and the feeding studies performed with N-acetyl glufosinate and glufosinate ammonium, no adjustment in ruminant and poultry tolerances are necessary.

OPPTS GLN 860.1500: Crop Field Trials

9a. ***Canola:*** The petitioner has requested a canola seed tolerance of 0.4 ppm for the combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate. The petitioner indicated that only the spring variety of canola has been genetically modified for tolerance to glufosinate ammonium. In Region 2, canola is only planted in the winter months (winter variety of canola) due to the unfavorable climate for canola in the summer. Therefore, the petitioner is not requesting registration for application of glufosinate ammonium to transgenic canola in Region 2.

9b. Two canola field trial studies conducted in Canada were submitted (MRID 443586-08 & -09). The field portion of MRID 443586-08 was not conducted according to GLP standards. The deficiencies which lead to nonconformance were not provided. Information pertaining to the application date, method, equipment, volume, timing and rate were provided. Therefore, the factors that lead to nonconformance with GLP standards will be considered minor and the study is acceptable. The field trial data conducted as part of MRID 443586-09 is also acceptable.

The combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate in/on transgenic canola seed following a single application of glufosinate ammonium at 0.9x or 1.3x the maximum proposed seasonal use rate ranged from <0.15 - <0.336 ppm (treated at 3-7 leaf stage; PHI = 57 - 83 days).

9c. According to Table 5 of OPPTS GLN 860.1500, a total of 8 trials conducted in Regions 2 (n=1, not necessary for this petition), 5 (n=2), 7 (n=2) and 11 (n=3) are suggested. The Canadian field trial data submitted with this petition can be applied to the following Regions (HED SOP 98_2); Region 7 (n=2) and Region 14 (n=12; Region 14 is unique to Canada). The issue of how to apply canola field trial data from Region 14 to a US Registration was brought to Chem SAC. B. Schneider gathered information on canola production in the US and Canada and concluded that the majority of US canola is grown in ND, MN, MT, WA and SD. Generally within these states the northern most counties are the highest producing areas of the state. The canola production in Region 11 has decreased and increased in Regions 5 and 7 since the guidelines were written. The SAC agreed on accepting the Canadian canola field trials for glufosinate ammonium due to the similarities between the US canola production areas and Region 14 (Minutes of 17-Jun-1999 ChemSAC meeting). Geographical distribution of the submitted field trials is adequate for establishment of a tolerance in/on canola. HED concludes that based on the submitted field trial data, the petitioners proposed tolerance of 0.4 ppm is appropriate.

9d. ***Sugar Beet:*** The petitioner has requested a sugar beet top tolerance of 1.3 ppm and a sugar beet root tolerance of 0.7 ppm for the combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate expressed as glufosinate free acid equivalents.

9e. The two submitted sugar beet field trial studies are adequate (MRIDs 443586-02 and -03). The combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate in/on transgenic sugar beet tops and roots treated with Liberty™ Herbicide at 1.1x - 1.5x the maximum proposed seasonal use rate ranged from <0.10 -1.30 ppm (tops) and <0.10 -

<0.830 ppm (roots). Pre-harvest intervals ranged from 41 - 139 days. Only 4 of the 14 field trials had a pre-harvest interval less than 80 days (label specifies a PHI = 60 days). The label indicates that the product may be applied from the cotyledon to 10 leaf stage of the sugar beet. The final application for all field trials was either at the 8 or 10 leaf stage and samples were harvested when the crop reached maturity. Since crop harvest was governed by crop development and the increased PHIs were counteracted in some cases by application rates 1.5x the maximum proposed rate, HED concludes that the field trial data are acceptable. Geographical distribution of the submitted field trials is adequate for establishment of a tolerance in/on sugar beets.

9f. HED concludes that based on the submitted field trial data, the appropriate tolerance in/on sugar beet tops and roots, as result of the application of glufosinate ammonium as defined in this petition, is 1.5 ppm and 0.9 ppm, respectively. The petitioner must submit a revised Section F proposing a 1.5 ppm tolerance in/on sugar beet tops and a 0.9 ppm tolerance in/on sugar beet roots for the combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate expressed as glufosinate free acid equivalents.

9g. *Potato:* The petitioner has requested a potato tolerance of 0.4 ppm for the combined residues of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents.

9h. The submitted potato field trial study is adequate (MRID 44583901). The combined residues of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid in/on potatoes treated with Rely® Herbicide at 1.1x the maximum proposed seasonal use rate (PHI = 9-10 days) ranged from <0.10 - <0.667 ppm. Geographical distribution of the submitted field trials is adequate for establishment of a tolerance in/on potatoes.

9i. HED concludes that based on the submitted field trial data, the appropriate tolerance in/on potatoes, as result of the application of glufosinate ammonium as defined in this petition, is 0.8 ppm. The petitioner must submit a revised Section F proposing a 0.8 ppm tolerance in/on potatoes for the combined residues of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents.

OPPTS GLN 860.1520: Processed Food/Feed

10a. *Canola:* The petitioner has requested a canola meal tolerance of 2.0 ppm for the combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate expressed as glufosinate free acid equivalents.

10b. The submitted canola processing study is adequate (MRID 44358610). Canola seed harvested 70 days after treatment with glufosinate ammonium at 0.67, 1.3 or 3.3 lbs ai/acre/application (0.9x, 1.7x and 4.3x the maximum seasonal application rates; treated at 4-6 leaf stage) was processed into meal, oil and soapstock. The combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate did not concentrate in oil or soapstock but did concentrate 3.4x and 2.9x in toasted meal (average 3.2x).

The highest field trial for canola seed was <0.336 ppm (Indian Head, Sk; MRID 44358609). The maximum combined glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate residue expected in/on transgenic canola meal, based on the highest field trial and the 3.2x concentration factor, is 1.1 ppm.

10c. HED concludes that the appropriate tolerance in/on canola meal, as a result of the application of glufosinate ammonium to canola as defined in this petition, is 1.1 ppm. The petitioner must submit a revised Section F proposing a canola meal tolerance of 1.1 ppm for the combined residues of glufosinate ammonium and its metabolites N-acetyl glufosinate ammonium and 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents.

10d. ***Sugar Beet:*** The petitioner has requested a sugar beet molasses tolerance of 5.0 ppm for the combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate expressed as glufosinate free acid equivalents.

10e. Sugar beets treated three times with Liberty™ Herbicide (2-leaf stage, 6-leaf stage and 8-leaf stage) at 2.5 - 2.7 lbs ai/acre/application (total applied 7.9 lbs ai/acre; 8.3x the maximum proposed seasonal application rate) were harvested 136 days after the final treatment and processed into pulp, molasses and sugar. The combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate did not concentrate in pulp or sugar but did concentrate 6.8x in molasses. Unprocessed sugar beet samples were stored for 5 months prior to analysis (adequate storage stability study covers this interval). Processed samples were stored for 3 months prior to analysis. No storage stability data for sugar beet pulp, molasses or sugar have been submitted.

The highest average field trial (HAFT) for sugar beet roots was 0.719 ppm (Fayette, OH; MRID 44358603). The maximum combined glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate residue expected in sugar beet molasses, based on the HAFT and the 6.8x concentration factor, is 5.0 ppm.

10f. HED will not be opposed to conditional registration of glufosinate ammonium on transgenic sugar beets. Unconditional registration may be granted upon validation of the three month storage interval for the processed commodities (sugar, pulp and molasses). Pending submission and evaluation of this data, HED concludes that the petitioners proposed sugar beet molasses tolerance of 5.0 ppm is appropriate.

10g. ***Potato:*** The petitioner has requested a potato flake tolerance of 1.3 ppm and a processed potato tolerance of 1.0 ppm for the combined residues of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents.

10h. The submitted potato processing study is adequate (MRID 44358612). Potatoes harvested 9 days after a single treatment with glufosinate ammonium at 2.0 lbs ai/acre (5.3x the maximum proposed single and seasonal application rate) were processed into chips, flakes and peel. The combined residues of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid did not concentrate in the peel but did concentrate 2.3x in potato chips and 3.0x in potato flakes.

The HAFT for potatoes was 0.662 ppm (Lee, FL; MRID 44583901). The maximum combined glufosinate ammonium and 3-methylphosphinico propionic acid residue expected in potato flakes, based on the HAFT and the 3.0x concentration factor, is 2.0 ppm. The maximum combined glufosinate ammonium and 3-methylphosphinico propionic acid residue expected in potato chips, based on the HAFT and the 2.3x concentration factor, is 1.6 ppm.

10i. HED concludes that the appropriate tolerance in/on potato chips and potato granuales/flakes, as a result of the application of glufosinate ammonium to potatoes as defined in this petition, is 1.6 ppm and 2.0 ppm, respectively. The petitioner must submit a revised Section F proposing a potato chip tolerance of 1.6 ppm and a potato granule/flake tolerance of 2.0 ppm for the combined residues of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents.

OPPTS GLN 860.1850 & 860.1900: Confined/Field Accumulation in Rotational Crops

11. The submitted label indicates a 120 day plant back interval for wheat only. The label should be amended to indicate a 120 day plant back interval for all crops except wheat where a 70 day plant back interval is appropriate.

Other Considerations

13. Codex currently has MRLs for the combined residues of glufosinate ammonium and and 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents in/on potatoes and sugar beets at 0.5 and 0.05 ppm, respectively (no MRLs established for canola). Canada currently has MRLs for the combined residues of glufosinate ammonium and 3-methylphosphinico propionic acid in/on potatoes and canola at 0.4 ppm and 3.0 ppm, respectively (no MRLs established for sugar beets). No glufosinate ammonium MRLs have been established in/on potatoes, sugar beets or canola in Mexico.

    The Canadian MRL for canola seed is greater than two times the appropriate US tolerance for canola seed; therefore, harmonization is not possible. Since the appropriate US tolerance for sugar beets and potatoes are greater than the Canadian and Codex MRLs, harmonization is not possible.

RECOMMENDATIONS

HED will not be opposed to conditional registration of glufosinate ammonium on transgenic sugar beets. Unconditional registration may be granted upon submission and evaluation of the information specified in conclusions 2a, 2c, 5d, 9f and 10f. HED concludes that the following tolerances for the combined residues of glufosinate ammonium, N-acetyl glufosinate and 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents, as a result of the application of glufosinate ammonium to transgenic sugar beets as defined in the petition, are appropriate:

Sugar Beet, Top .... 1.5 ppm
Sugar Beet, Root .... 0.9 ppm
Sugar Beet, Molasses .... 5.0 ppm

HED will not be opposed to conditional registration of glufosinate ammonium on transgenic canola. Unconditional registration may be granted upon submission and evaluation of the information specified in conclusions 2b, 2c, 5d and 10c. HED concludes that the following tolerances for the combined residues of glufosinate ammonium, N-acetyl glufosinate and 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents, as a result of the application of glufosinate ammonium to transgenic canola as defined in this petition, are appropriate:

Canola Seed .... 0.4 ppm
Canola, Meal .... 1.1 ppm

HED will not be opposed to conditional registration of glufosinate ammonium on potatoes. Unconditional registration may be granted upon submission and evaluation of the information specified in conclusions 2c, 5d, 9i and 10i. HED concludes that the following tolerances for the combined residues of glufosinate ammonium and 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents, as a result of the application of glufosinate ammonium to potatoes as defined in this petition, are appropriate:

Potato .... 0.8 ppm
Potato, chip .... 1.6 ppm
Potato, granules/flakes .... 2.0 ppm

A human-health risk assessment will be prepared as a separate document.

DETAILED CONSIDERATIONS

OPPTS GLN 830 Series: Product Properties

Product chemistry data for glufosinate ammonium has been submitted, reviewed and found acceptable. No additional product chemistry data is necessary for this petition (PP#8F3607, J. Garbus, 14-Oct-1988 and 8-Aug-1990).

The active ingredient in the technical and formulated products is identified as glufosinate ammonium and concentrations are reported in terms of the racemic mixture.

OPPTS GLN 860.1200: Directions for Use

The petitioner is requesting registration of Liberty™ Herbicide (18.19% glufosinate ammonium; 1.67 lbs ai/US gallon; EPA Reg. No. 45639-199) for use on the transgenic varieties of sugar beet and canola and Rely® Herbicide (11.33% glufosinate ammonium; 1.00 lbs ai/US gallon; EPA Reg. No. 45639-187) for use in potato vine dessication. Both products are water-soluble and applied as a foliar spray. The Liberty™ label indicates that a 120 day interval from the last application is required prior to planting wheat and grazing treated crop or cut for hay is prohibited.

Sugar Beets: Applications of Liberty™ Herbicide may be made from the cotyledon stage up to the 10 leaf stage. Maximum recommended single application rate is 0.48 lbs ai/acre. A maximum of 0.95 lbs ai/acre can be applied per season. Application can be made with ground (controlled droplet application equipment or air assisted spray equipment; minimum of 10 gallons of water/acre) or aerial (minimum of 5 gallons of water/acre) equipment. The label specifies a 60 day pre-harvest interval (PHI).

Canola: Applications of Liberty™ Herbicide may be made from the cotyledon stage up to the early bolting stage (at this stage the plant has at least 6 leaves). A maximum of two applications per season is allowed with the total seasonal rate not to exceed 0.77 lbs ai/acre. Application can be made with ground (controlled droplet application equipment or air assisted spray equipment; minimum of 10 gallons of water/acre) or aerial (minimum of 5 gallons of water/acre) equipment. The label specifies a 65 day PHI.

Potato: Application of Rely® Herbicide is recommended at the beginning of natural vine senescence. The product is to be applied at a rate of 0.375 lbs ai/acre in 20-100 gallons of water per acre with ground equipment or in 5-10 gallons of water per acre with aerial equipment. The label specifies a 9 day PHI. Potatoes grown for seed stock are not to be treated.

Conclusion: The sugar beet portion of the Liberty™ Herbicide label should be amended to indicate in the "Special Notes" section that the maximum single application rate is 42 fluid ounces/acre (0.48 lbs ai/acre).

The maximum seasonal application rate for canola is listed as 0.77 lbs ai/acre in the application timing section and 0.73 lbs ai/acre in the special notes section (0.77 lbs ai/acre will be assumed to be correct). The petitioner indicated that only the spring variety of canola has been genetically modified for tolerance to glufosinate ammonium. In Region 2, canola is only planted in the winter months (winter variety of canola) due to the unfavorable climate for canola in the summer. Therefore, the petitioner is not requesting registration of transgenic canola in Region 2. The canola portion of the Liberty™ Herbicide label should be amended to indicate in the "Special Notes" section that use of this product on transgenic canola in Region 2 is prohibited.

Both the Rely® Herbicide and Liberty™ Herbicide labels should be amended to indicate a 120 day plant back interval for all crops except wheat where a 70 day plant back interval is appropriate.

OPPTS GLN 860.1300: Nature of the Residue - Plants

SUGAR BEETS

MRID 44358601: C^{14}-Labeled Glufosinate-ammonium (Hoe 039866) Metabolism in Genetically Modified Sugar Beets (Beta *vulgaris* ssp *vulgaris* var *altissima*) After Two Applications of C^{14}-Glufosinate-Ammonium at a Rate of 600 g ai/ha Each: The in-life and analytical phases of the study were conducted by Hoechst Schering AgrEvo GmbH (Frankfurt, Germany). 3,4[C^{14}]Glufosinate-ammonium (specific activity 52,413 dpm/µg, radiochemical purity 98.3%) was applied to transgenic sugar beets as a foliar spray 35 and 57 days after planting at 600 g ai/ha (0.54 lbs ai/acre, 1.1x proposed maximum single application rate); the total application rate was 1.2 kg ai/ha (1.07 lbs ai/acre; 1.1x the proposed maximum seasonal rate). Samples were collected 0, 8, and 15 days following the first application, 0 and 21 days following the second application, and at maturity (146 days following the second application). The plants were divided into leaves (tops) and beets (when formed). Leaves were rinsed with water and the water rinse collected

Extraction and Characterization of Residues: The root and rinsed leaves were homogenized. Radioactivity in rinses and homogenate were determined by LSC or combustion/LSC (limit of quantitation (LOQ) = 0.0011 ppm). The petitioner also determined TRR by summing the radioactivity in extracts and solids following extraction. Both TRR values are summarized in Table1. The petitioner used the summed TRR values for all subsequent calculations.

Table 1: TRR in transgenic sugar beet

	TRR, ppm [^{14}C]glufosinate-ammonium equivalents					
	0 day PHI [1]		21 day PHI		146 day PHI	
Commodity	Combustion [2]	Extraction [3]	Combustion [2]	Extraction [3]	Combustion [2]	Extraction [3]
Rinse	11.95	11.95	1.68	1.68	0.06	0.06
Tops	8.30	8.14	9.62	10.58	2.02	1.99
Total (tops)	20.25	20.08	11.30	12.26	2.08	2.05
Roots	1.97	2.01	6.47	6.75	0.84	0.93

1 PHI = preharvest interval; days from second treatment
2 TRR determined by combustion of entire sample
3 TRR determined by summing radioactivity in extracts and solids remaining following extraction

The 0, 21 and 146 day (days after second treatment) homogenized sugar beet top and root samples were extracted with a water/methanol solution (90/10 v/v) and centrifuged. The supernatant was isolated and the extraction was repeated until greater than 95% of TRR had been extracted, or the extract contained less than 2% of the TRR. Extracts were concentrated and reserved for HPLC and TLC analysis.

HPLC analysis were conducted using a Spherisorb SAX (strong basic anion exchange) column and an isocratic mobile phase of phosphoric acid/potassium dihydrogen phosphate (5 mM, pH = 2) and methanol (System 1 - 90:10 (v:v); System 2 - 30:70 (v:v)). The petitioner claimed that the two different solvent systems separated the analytes by two different mechanisms: System 1 by ion-exchange chromatography and System 2 by adsorption chromatography. Radioactivity was detected and quantified using a radioactivity monitor. The petitioner attempted to conduct TLC analysis to confirm identifications of metabolites. However, matrix effects prevented good separation of metabolites.

Therefore, identification of metabolites was confirmed by identification and quantification in HPLC systems 1 and 2. The distribution of radioactive residues in the water rinse, rinsed leaves and roots are summarized in Table 2. A summary of the characterized and identified ^{14}C-residues in sugar beet commodities are presented in Table 3 (see attachment 1 for structures of identified compounds).

The petitioner also extracted and analyzed crop samples collected after the first treatment but before the second treatment. The rinsates of plants collected 3 hours, 8 days and 15 days following the first treatment contained glufosinate ammonium at 40.5%, 18.8% and 13.8% TRR in tops, respectively. Isomeric separation (using HPLC with a Crompak CR column) demonstrated equal proportions of D and L isomers in the rinsates from all PHIs. In the homogenate extract of tops collected 3 hours after the first treatment, 45.1% of TRR was parent and 9.0% TRR was N-acetyl glufosinate. In the homogenate extract of tops collected 15 days after the first treatment, 29.3% of TRR was parent and 48.6% of TRR was N-acetyl glufosinate. Isomeric separation of the parent peak from the homogenate extracts (tops) demonstrated equal proportions of the D and L isomers on day 0. However, by 15 days following treatment, the D isomer of the parent accounted for 25.2% of TRR and the L-isomer accounted for 3.3% of TRR, indicating that acetylation of glufosinate-ammonium in the transgenic plants occurs with the L isomer only.

Storage Stability: Samples of sugar beet commodities were stored frozen prior to analysis. The petitioner stated that samples were extracted and analyzed within 30 days of harvest except for 0-day PHI root samples which were stored for over 30 days prior to analysis (exact storage interval not provided). Leave and root samples (PHI = 146 days) were stored frozen for 3 months and extracted and analyzed a second time. The initial extract and the extract from the samples stored three months were qualitatively and quantitatively similar indicating that glufosinate ammonium residues in/on sugar beet roots and leaves are stable for 3 months when stored frozen.

Table 2: Distribution and characterization radioactive residues in transgenic sugar beet

Fraction	% TRR	ppm	Characterization/Identification		
0 day PHI Tops (TRR = 20.08 ppm)					
Rinsate	59.50	11.95	Glufosinate-ammonium	59.4% TRR	11.92 ppm
Water:methanol	39.47	7.93	Glufosinate-ammonium MP-propionic acid N-acetyl-glufosinate	25.2% TRR 0.4% TRR 13.4% TRR	5.05 ppm 0.07 ppm 2.68 ppm
Nonextractable	1.03	0.21	Not further analyzed (N/A).		
0 day PHI Roots (TRR = 2.01 ppm)					
Water:methanol	97.39	1.95	Glufosinate-ammonium MP-propionic acid N-acetyl-glufosinate	30.9% TRR 2.2% TRR 64.3% TRR	0.62 ppm 0.04 ppm 1.28 ppm
Nonextractable	2.61	0.05	N/A.		
21 day PHI Tops (TRR = 12.26 ppm)					
Rinsate	13.68	1.68	Glufosinate-ammonium	13.7% TRR	1.68 ppm
Water:methanol	85.03	10.42	Glufosinate-ammonium MP-propionic acid N-acetyl-glufosinate	28.1% TRR 1.1% TRR 55.2% TRR	3.44 ppm 0.13 ppm 6.77 ppm
Nonextractable	1.29	0.16	N/A.		

Fraction	% TRR	ppm	Characterization/Identification		
21 day PHI Roots (TRR = 6.75 ppm)					
Water:methanol	96.39	6.50	Glufosinate-ammonium	30.6% TRR	2.07 ppm
			MP-propionic acid	2.0% TRR	0.14 ppm
			N-acetyl-glufosinate	63.3% TRR	4.27 ppm
Nonextractable	3.61	0.24	N/A.		
146 day PHI Tops (TRR = 2.05 ppm)					
Rinsate	3.01	0.06	Glufosinate-ammonium	2.3% TRR	0.05 ppm
			MP-propionic acid	0.3% TRR	0.006 ppm
			N-acetyl-glufosinate	0.2% TRR	0.005 ppm
			2-methylphosphinico-acetic acid	0.07% TRR	0.001 ppm
			Plus 1 unknown peak	0.09% TRR	0.002 ppm
Water:methanol	94.48	1.94	Glufosinate-ammonium	24.0% TRR	0.49 ppm
			MP-propionic acid	2.7% TRR	0.055 ppm
			N-acetyl-glufosinate	66.9% TRR	1.37 ppm
Nonextractable	2.51	0.05	N/A.		
146 day PHI Roots (TRR = 0.93 ppm)					
Water:methanol	96.25	0.89	Glufosinate-ammonium	19.1% TRR	0.18 ppm
			MP-propionic acid	6.0% TRR	0.055 ppm
			N-acetyl-glufosinate	67.9% TRR	0.63 ppm
			Plus 1 unknown peak	3.1% TRR	0.03 ppm
Nonextractable	3.75	0.03	N/A.		

Table 3: Summary of radioactive residues characterized/identified in transgenic sugar beet

Fraction	0 Day PHI Tops (TRR = 20.08 ppm)		21 Day PHI Tops (TRR = 12.26 ppm)		146 Day PHI Tops (TRR = 2.05 ppm)		0 Day PHI Roots (TRR = 2.01 ppm)		21 Day PHI Roots (TRR = 6.75 ppm)		146 Day PHI Roots (TRR = 0.93 ppm)	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm
Identified [1]												
Glufosinate-ammonium	84.6	16.97	41.8	5.12	26.3	0.54	30.9	0.62	30.6	2.07	19.1	0.18
MP-propionic acid	0.4	0.07	1.1	0.13	3.0	0.061	2.2	0.04	2.0	0.14	6.0	0.055
N-acetyl-glufosinate	13.4	2.68	55.2	6.77	67.1	1.38	64.3	1.28	63.3	4.27	67.9	0.63
2-methylphosphinico-acetic acid	--	--	--	--	0.07	0.001	--	--	--	--	--	--
Total identified	**98.4**	**19.72**	**98.1**	**12.02**	**96.5**	**1.98**	**97.4**	**1.94**	**95.9**	**6.48**	**93.0**	**0.87**
Unknown	--	--	--	--	0.09	0.002	--	--	--	--	3.1	0.03
Nonextractable	1.03	0.21	1.29	0.16	2.51	0.05	2.61	0.05	3.61	0.24	3.75	0.03

[1] See Attachment 1 for chemical structures of identified metabolites.

Sugar Beet Metabolism Summary: The qualitative nature of glufosinate ammonium residues in transgenic sugar beets is adequately understood. Total radioactive residues (TRR) were 2.05 ppm in tops and 0.93 ppm in roots harvested 146 days following the last of 2 applications of [C^{14}]glufosinate-ammonium at 0.54 lbs ai/acre (total application rate 1.07 lbs ai/acre, 1.1x the maximum proposed single and seasonal application rates). Samples of sugar beet commodities were also collected at shorter preharvest intervals (PHIs); TRR were 20.08 ppm in tops and 2.01 ppm in roots collected 1 hour after the second application and were 12.26 ppm in tops and 6.75 ppm in roots collected 21 days after the second application.

In sugar beet tops and roots (all PHIs), 93-98% of the TRR was identified. The N-acetyl glufosinate metabolite was the major residue in all sugar beet top and root samples (55.2-67.9% TRR), except 0-day PHI tops where glufosinate ammonium accounted for 84.6% of the TRR (N-acetyl glufosinate accounted for 13.4% of the TRR). Glufosinate-ammonium accounted for 19.1-41.8% of the TRR in all other sugar beet top and root samples. 3-Methylphosphinico propionic acid was identified at low levels in all sugar beet samples (0.4-6.0% TRR). One additional metabolite, 2-methylphosphinico acetic acid, was identified in 146 day PHI tops at 0.07% TRR.

The current tolerance expression for commodities derived from transgenic crops includes the major residues identified in the transgenic sugar beet metabolism study and is adequate for commodities derived from transgenic sugar beets. The residues of concern in/on transgenic sugar beets are glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate.

CANOLA

MRID 443586-06 & -07: (Carbon-14)-Glufosinate-Ammonium: Nature of Seed Residue in Transgenic Canola (Rapeseed): The in-life phase of the study was conducted by Research for Hire (Porterville, CA) and the analytical phase of the study was conducted by Hazleton Wisconsin, Inc. (Madison, WI). 3,4[C^{14}]Glufosinate-ammonium (specific activity 20.62 mCi/g, radiochemical purity 98%) was applied to canola plants at the 3-5 leaf stage as a foliar spray at 0.75 kg ai/ha (0.67 lbs ai/acre; 0.9x the proposed maximum seasonal rate). Samples were collected 1 hour postreatment, 21 days posttreatment and at maturity (120 days posttreatment). The 1 hour post application sample was collected as a whole sample. The 21 day sample was separated into top growth and roots. The 120 day sample was separated into roots, top growth and seed pods (seeds and hulls). Plants were separated into top growth (foliage) and roots by cutting approximately 0.5 - 1 inch above the soil. The roots (21 day and 120 day samples) and foliage (120 day samples) were separately rinsed with water (twice). Seed pods were rinsed with water (twice) and separated by hand into seeds and hulls. Samples, including rinsates, were stored frozen (-20 C) until analysis.

Extraction and Characterization of Residues: The rinsed hull, seed, stalk and root samples were homogenized. Radioactivity in the rinses and homogenate were quantified by LSC or combustion/LSC (limit of detection (LOD) = 0.005 ppm). Radioactivity in rinsate samples were not expressed in terms of radioactivity in the crop commodity. The radioactivity in the hull and foliage rinsates from the 120 day treated samples were essentially the same as that attained for control samples. The TRR in canola commodities are presented in Table 4.

Table 4: TRR in transgenic canola

Commodity	TRR, ppm [^{14}C]glufosinate-ammonium equivalents		
	1 hour PHI	21 day PHI	120 day PHI
Whole plant	144.578	--	--
Foliage (top growth)	--	3.207, 5.343	0.021, 0.024, 0.058, 0.064
Roots	--	3.807, 5.192	0.134, 0.150, 0.187, 0.220
Hulls	--	--	0.076, 0.106, 0.125, 0.263
Seed	--	--	0.045, 0.054, 0.056, 0.109

Canola seed and hulls samples were subjected to sequential extraction with hexane, acetone and water/methanol (90:10, v/v). Non-extractable residues from canola seed were subjected to further extraction procedures to characterize nonextractable residues. Residues were first subjected to a second extraction with water:methanol (90:10, v:v). Water-soluble polysaccharides and proteins were extracted using 0.05 M dipotassium hydrogen phosphate buffer (4 hours at room temperature). Lipids were extracted using methanol:chloroform (2:1, v:v) and acetone. The remaining solids were acid hydrolyzed using 1 M hydrochloric acid (at 55 C for 90 minutes) and base hydrolyzed using 0.5 M sodium hydroxide (at 55 C for 45 minutes).

The homogenate from the 1 hour posttreatment sample (whole plant; root and foliage) as well as canola foliage homogenate collected 21 days posttreatment were extracted with water and centrifuged; the extraction was repeated three more times and extracts were combined for HPLC analysis.

HPLC analysis was conducted using either a Spherisorb SAX column and a gradient mobile phase of potassium dihydrogen phosphate buffer and methanol (System 1) or LC-8 and RX-C8 columns (in series) and an isocratic mobile phase of potassium dihydrogen phosphate buffer (System 2). Radioactivity was detected and quantified using fraction collection followed by LSC analysis. Seed and hull samples were analyzed using HPLC systems 1 and 2 (whole plant and foliage samples analyzed by system 1 only). Different levels of the parent and the 3-methylphosphinico propionic acid metabolite in extracts were observed depending on which system was used. No explanation was provided for this difference.

TLC analysis was conducted to confirm identification of metabolites. Radioactivity on TLC plates was detected and quantified using a signal analyzer and a digital autoradiography program. For seed and hull analysis, low levels of radioactivity and matrix effects prevented good separation of metabolites. Although there were some matrix effects, the presence of glufosinate-ammonium and N-acetyl-glufosinate in 1-hour PHI whole plant (root and foliage) and 21-day PHI foliage extracts were confirmed by TLC. A summary of the distribution and identification of metabolites in glufosinate tolerant canola is presented in Table 5 (see Attachment 1 for structures of identified metabolites).

Storage Stability: Samples were stored in a freezer within 24 hours of collection and remained frozen until analysis. Dates of extraction and analysis were not provided. Based on sample collection date and study completion date, samples of canola seed and hulls (MRID 44358606) were extracted and analyzed within 5 months of collection, and samples of whole plant and canola foliage (MRID 44358607) were extracted and analyzed within 19 months of collection.

A storage stability study performed on transgenic soybean demonstrated that glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate are stable for 12 months in soybean seed, forage and hay and for 3 months in soybean oil and meal (D211531 D219069, M. Rodriguez, 7-Mar-1996). This information is sufficient to support the storage conditions and intervals for canola seed and hull samples. The storage interval for whole canola plant and forage has not been validated.

Table 5: Distribution and characterization radioactive residues in transgenic canola

Fraction	% TRR	ppm	Characterization/Identification
1 Hour PHI Plant (TRR = 144.58 ppm)			
Water	98.9	142.97	HPLC analysis (System 1) resolved: Glufosinate-ammonium 72.9% TRR 105.4 ppm N-acetyl-glufosinate 18.2% TRR 26.3 ppm **Total identified 91.1% TRR 131.7 ppm**
Nonextractable	0.24	0.34	Not further analyzed (N/A).
21 Day PHI Foliage (TRR = 5.343 ppm)			
Water	99.2	5.30	HPLC analysis (System 1) resolved: Glufosinate-ammonium 20.7% TRR 1.11 ppm MP-propionic acid 6.7% TRR 0.358 ppm N-acetyl-glufosinate 60.2% TRR 3.22 ppm **Total identified 87.6% TRR 4.69 ppm**
Nonextractable	2.24	0.12	N/A.
120 Day PHI Seeds (TRR = 0.109 ppm)			
Hexane	4.5	0.005	N/A.
Acetone	6.6	0.007	N/A.
Water:methanol	55.7	0.061	HPLC analysis (System 1) resolved: Glufosinate-ammonium 10.8% TRR 0.012 ppm MP-propionic acid 26.8% TRR 0.029 ppm N-acetyl-glufosinate 8.6% TRR 0.009 ppm **Total identified 54.8% TRR 0.060 ppm** HPLC analysis (System 2) resolved: Glufosinate-ammonium 30.1% TRR 0.033 ppm MP-propionic acid 6.5% TRR 0.007 ppm **Total identified 36.7% TRR 0.040 ppm**
Nonextractable	37.8	0.041	Subjected to sequential extraction/hydrolysis procedures using water:methanol, phosphate buffer, methanol:chloroform, acetone, mild acid, and mild base.
Water:methanol	3.8	0.004	N/A.
Phosphate	12.4	0.014	N/A.
Methanol:chloroform	1.3	0.001	N/A.
Acetone	3.4	0.004	N/A.
Acid hydrolysate	4.9	0.005	N/A.
Base hydrolysate	4.8	0.005	N/A.

Fraction	% TRR	ppm	Characterization/Identification		
Nonextractable	6.9	0.008	N/A.		
120 Day PHI Hulls (TRR = 0.263 ppm)					
Hexane	ND	ND	N/A.		
Acetone	ND	ND	N/A.		
Water:methanol	77.1	0.203	<u>HPLC analysis (System 1) resolved:</u>		
			Glufosinate-ammonium	5.0% TRR	0.013 ppm
			MP-propionic acid	37.4% TRR	0.098 ppm
			N-acetyl-glufosinate	7.3% TRR	0.019 ppm
			Total identified	**49.7% TRR**	**0.131 ppm**
			<u>HPLC analysis (System 2) resolved:</u>		
			MP-propionic acid	44.8% TRR	0.118 ppm
			N-acetyl-glufosinate	13.9% TRR	0.037 ppm
			Total identified	**58.7% TRR**	**0.154 ppm**
			two unknowns	23.2% TRR	0.061 ppm
				2.3% TRR	0.006 ppm
Nonextractable	37.4	0.098	N/A.		

ND = not detected

Canola Metabolism Study Summary: Total radioactive residues (TRR) were 0.021-0.064 ppm in foliage, 0.134-0.220 ppm in roots, 0.076-0.263 ppm in hulls, and 0.045-0.109 ppm in seed harvested 120 days (at maturity) following a single application of [^{14}C]glufosinate-ammonium at 0.67 lbs ai/acre (0.9x the maximum proposed seasonal rate). Samples of canola commodities were also collected at shorter PHIs; TRR were 144.578 ppm in the entire plant collected at 1-hour PHI, and were 3.207 and 5.343 ppm in foliage, and 3.807 and 5.192 ppm in roots collected at 21-day PHI.

In the whole plant harvested 1 hour posttreatment, the parent accounted for the majority of the radioactivity (72.9% TRR, 105.4 ppm); N-acetyl-glufosinate was identified at 18.2% of the TRR (26.3 ppm). In foliage harvested 21 days posttreatment, the major residue was N-acetyl-glufosinate (60.2% TRR, 3.22 ppm); the parent was present at 20.7% of the TRR (1.11 ppm) and a small amount of 3-methylphosphinico propionic acid was identified (6.7% TRR, 0.358 ppm).

In mature canola seed and hulls (0.109 ppm and 0.263 ppm, respectively), 37-58% of the TRR was identified (the remainder of the extracted radioactivity was described as unknown metabolites equivalent to the LOD). Glufosinate-ammonium and 3-methylphosphinico propionic acid were the major residues identified, accounting for 5.0-44.8% of the TRR (0.007-0.118 ppm). The N-acetyl-glufosinate metabolite was a minor residue accounting for 1.1-13.9% of the TRR (0.001-0.037 ppm). In canola seed, radioactive residues associated with water-soluble polysaccharides and/or proteins accounted for 12.4% of the TRR (0.014 ppm).

The submitted study is marginally adequate to describe the nature of the residue in glufosinate tolerant canola. The test substance was applied at less than 1x the maximum proposed seasonal rate which resulted in low levels of radioactivity in canola seed, making identification of residues difficult. The storage interval prior to analysis and extraction of whole plant and canola foliage (19 months) were not within the validated time interval (12 months). Seed and hull samples were analyzed using HPLC systems 1 and 2 (whole plant and foliage samples analyzed by system 1 only). Different levels of parent, N-acetyl glufosinate and 3-methylphosphinico propionic acid were observed depending on which system was used. No explanation for this difference was provided. Since adequate metabolism studies on the transgenic varieties of field corn and soybeans have been previously submitted (D211531 and D219069, M. Rodriguez, 7-Mar-1996) and the results from the canola study do not significantly differ from these studies, no additional data pertaining to the metabolism of glufosinate-ammonium in transgenic canola are required. The residues of concern in/on transgenic canola are glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate.

POTATO

Nature of the Residue Potato: The nature of the residue is considered to be understood in genetically unaltered lettuce, soybeans, corn, apples and wheat. After application of ^{14}C glufosinate ammonium to the nutrient medium (water or soil) in which these crops were grown, only one labeled metabolite could be identified, 3-methylphosphinico propionic acid (parent was not found). HED concluded that the residues to be regulated in commodities derived from genetically unaltered lettuce, soybeans, corn, apples and wheat are glufosinate ammonium and 3-methylphosphinico propionic acid (PP#8F3607, J. Garbus, 8-Aug-1990).

A metabolism study has not been performed on a root vegetable (potato). Since the metabolism of glufosinate ammonium is consistent in four diverse crops groups (lettuce [leafy vegetable], soybeans [legume vegetable], wheat [cereal grain] and apple [fruit]) the nature of glufosinate ammonium residues in potatoes will be considered to be understood. The residues of concern in/on potatoes are glufosinate ammonium and 3-methylphosphinico propionic acid.

OPPTS GLN 860.1300: Nature of the Residue - Animals

The nature of glufosinate ammonium residues in lactating goats and hens is considered to be understood . It was shown that the glufosinate ammonium and its metabolite (3-methylphosphinico propionic acid) are largely excreted and do not accumulate too any great degree in animal tissues. The only identifiable compounds in feces, urine, milk, eggs and tissues were the parent and 3-methylphosphinico propionic acid. HED concluded that the residues of concern in commodities derived from ruminants and poultry are glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid (PP#8F3607, J. Garbus, 8-Aug-1990).

Transgenic field corn, soybeans, canola and sugar beets contain a second metabolite, N-acetyl glufosinate, which may lead to secondary residues of this compound in animal commodities. Feeding studies conducted on dairy cows and laying hens were submitted and reviewed as part of glufosinate ammonium registration on transgenic field corn and transgenic soybeans. In these studies, dairy cows and hens were feed a diet consisting of glufosinate ammonium and N-acetyl glufosinate. It was determined, that the tolerance expression for poultry (new tolerance as a result of registration on transgenic soybeans and transgenic field corn) should include glufosinate ammonium and 3-methylphosphinico propionic acid (N-acetyl glufosinate should not be included; D232571, M. Rodriguez). Additionally, it was determined that the currently established egg, milk, and fat, meat, and meat byproducts tolerances on cattle, goats, hogs, horses, poultry, and sheep were adequate (D211531 and D219069, M. Rodriguez, 7-Mar-1996).

OPPTS GLN 860.1340: Residue Analytical Method

Analytical methodology is available in PAM II for determination of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid in genetically unaltered apples, bananas, grapes and tree nuts (HRAV-5A) and in milk, eggs and the tissues of ruminants and poultry (HRAV-12, also called BK/01/95). Method HRAV-5A employs extraction of glufosinate ammonia and its metabolite 3-methylphosphinico propionic acid from a 25 gram homogenized sample with water. The aqueous extract is filtered and subjected to anion-exchange chromatography for removal of interfering compounds. The residues are eluted from the resin with formic acid and derivatized by refluxing with trimethylorthoacetate. The derivatized residues are cleaned up on a silica gel column and quantified by GC/FPD. All compounds are quantified in terms of glufosinate free acid equivalents. Method HRAV-12 (used to determine residue levels in animal matrices) is similar to the plant method except for an addition step. Water extracts of tissues are diluted with acetone to precipitate protein, centrifuged and then subjected to anion ion-exchange chromatography.

In transgenic crops a second metabolite, N-acetyl glufosinate, is present. Since glufosinate ammonium and N-acetyl glufosinate are derivatized to the same compound, HRAV-5A does not distinguish between these two compounds. A second method, AE-24, was developed for individual determination of the three compounds regulated in commodities derived from transgenic crops. Method AE-24 is a modification of the current analytical enforcement method (HRAV-5A) in that following anion exchange, cation exchange is performed. Two fractions are collected from the cation ion exchange column. One fraction contains N-acetyl glufosinate and 3-methylphosphinico propionic acid and the second fraction contains glufosinate ammonium. Each fraction is derivatized by refluxing with trimethylorthoacetate, cleaned up on a silica gel column and quantified by GC/FPD.

Several variations of these two methods were used for quantitation of residues in the submitted field trials; all of which are adequate for data gathering purposes. The petitioner also submitted a brief description of a GC/MS confirmatory technique. Validation data was not conducted for all methods and/or matrices. However, concurrent recovery data demonstrated the adequacy of each method in all necessary matrices.

Table 6: Validation Recoveries

commodity	fortification (ppm)	% recovery[1]		
		HOE 039866[2]	HOE 099730[2]	HOE 061517[2]
canola seed HRAV-24 MRID 44358608	0.05-0.20	80.2-87.6 (3), **84.0**	70.5-88.9 (3), **79.7**	83.5-107 (3), **97.8**
canola seed XAM-24 MRID 44358609	0.05-0.20	83.5-107 (3), **97.8**	80.2-87.6 (3), **84.0**	70.5-88.9 (3), **79.7**
canola soapstock HRAV-24 MRID 44358610	0.05-0.20	89.0, 106; **97.5**	117, 135; **126**	105, 104; **105**
Potato; XAM-24B; MRID44358612				
potato[3]	0.05 - 3.0	79.0 ± 5.3 (6)	*	97.2 ± 5.5 (6)

commodity	fortification (ppm)	% recovery[1]		
		HOE 039866 [2]	HOE 099730 [2]	HOE 061517 [2]
chips	0.05 - 0.50	72.4-98.7 (10); **85.0**	*	86.6-107 (10); **97.9**
flakes	0.05 - 0.50	72.1-99.4 (10); **86.9**	*	77.3-103 (10); **90.9**
wet peel	0.05- 0.50	80.2-113 (10); **96.8**	*	75.3-97.3 (10); **90.8**

[1] range of recoveries; number of samples in parenthesis; average in bold
[2] HOE 039866 = glufosinate ammonium, HOE 099730 = N-acetyl glufosinate, HOE 061517 = 3-methylphosphinico propionic acid
[3] only average and std dev was given for potatoes
* non-transgenic crop; N-acetyl glufosinate is not a metabolite

Table 7: Concurrent Recoveries

commodity	fortification (ppm)	% recovery[1]		
		HOE 039866 [2]	HOE 099730 [2]	HOE 061517 [2]
canola seed HRAV-24 MRID 44358608	0.05-0.20	74.0-87.0 (8), **80.3**	87.4-119 (8), **97.7**	71.6-107 (8), **83.2**
canola seed XAM-24 MRID 44358609	0.05-0.10	69.3-99.0 (6), **85.3**	95.0-120 (6), **108**	91.6-117 (6), **105**
canola; HRAV-24; MRID 44358610				
canola seed	0.05	91.8	109	111
crude oil	0.05	74.1	99.9	96.2
untoasted meal	0.20	99.7	76.2	99.4
toasted meal	1.00	96.6	91.8	106
refined oil	0.05	91.8	120	89.6
refined bleached oil	0.10	92.4	97.0	91.5
refined bleached deodorized oil	0.05	84.1	91.6	70.0
soapstock	0.05	108	127	107
sugar beet; BK/04/95; MRID 44827901 (storage stability study)				
tops	0.25	51.9, 60.8, 68.8, 70.6-80.2 (3), **67.6**	49.6, 70.0-85.8 (5), **72.6**	79.4-118 (10), **98.1**

commodity	fortification (ppm)	% recovery[1]		
		HOE 039866[2]	HOE 099730[2]	HOE 061517[2]
root	0.25	63.8, 79.8-108 (6), **85.2**	82.2-110 (6), **95.9**	73.2-115 (11), **93.7**
sugar beet; BK/04/95; MRID 44358602				
tops and crown	0.05-4.0	73.6-96.3 (9), **83.6**	72.6-117 (18), **86.4**	73.1-114 (9), **83.3**
root	0.05-0.10	87.4-108(5), **98.2**	75.9-112 (10), **91.4**	80.6-96.2 (5), **87.7**
sugar beet; BK/04/95; MRID 44358603				
tops and crown	0.05-1.00	74.2-109 (9), **88.9**	85.6-119 (18), **101**	68.0, 70.1-103 (8), **84.4**
root	0.05-1.00	82.7-117 (10), **96.4**	67.1, 72.8-105 (19), **87.7**	77.4-101 (10), **88.8**
sugar beet; BK/04/95; MRID 44358604				
roots	0.05 - 2.00	87.3; fortified at 0.50	100, 92.5; **96.3** fortified at 0.05 & 2.00	68.0, 87.9, 113; **89.6**
dried pulp	0.05 - 2.00	78.3; fortified at 0.50	104, 107; **106** fortified at 0.05 and 1.00	79.8 - 108 (3); **92.0**
molasses	0.05, 10.0	86.3; fortified at 0.05	88.1, fortified at 10.0	74.0, 106; **90.0**
refined sugar	0.05, 10.0	90.8; fortified at 10.0	94.4, fortified at 0.05	91.3, 111; **101**
potato; XAM-24B; MRID 44358612				
tubers	0.05, 2.50	84.3-89.4 (3); **87.2**	*	86.4-95.9 (3); **90.3**
chips	0.05, 2.00	88.5, 93.5; **91.0**	*	94.0, 102; **98.0**
flakes	0.05, 2.00	89.9, 105; **97.5**	*	85.8, 96.4; **91.1**
wet peel	0.05, 2.50	80.9, 88.9; **84.9**	*	81.9, 92.9; **87.4**
potato; BK/05/95 MRID 44583901	0.05-0.80	92.9-120 (11), **120**	*	88.0-102 (11), **97.0**

1 range of recoveries; number of samples in parenthesis; average in bold
2 HOE 039866 = glufosinate ammonium, HOE 099730 = N-acetyl glufosinate, HOE 061517 = 3-methylphosphinico propionic acid

Conclusions: A complete description of the GC/MS confirmatory technique should be submitted by the petitioner.

Two of the methods used for quantification of residues in the field trials, BK/04/95 (used for quantitation of residues in/on transgenic sugar beet commodities) and HRAV-24 (used for quantitation of residues in/on transgenic canola commodities), were submitted to the Analytical Chemistry Branch (ACB) for Petition Method Validation (D254830, T. Bloem, 1-Apr-1999). Method BK/04/95 is similar to the current analytical enforcement method HRAV-5A but with modifications for application to a root crop. Method HRAV-24, which employs the cation exchange fractionation procedure (cation exchange procedure has not undergone Agency validation), was submitted to ACB for validation.

Given that the registrant has provided concurrent fortification data to demonstrate that BK/04/95 and HRAV-24 are adequate for data collection purposes and these methods are a modification of the current tolerance enforcement method, HED concludes that they are suitable enforcement methods to support tolerances associated with a conditional registration on potatoes, transgenic sugar beets and transgenic canola. As a condition of the registration, HED will require a successful petition method validation and the registrant will be required to make any necessary modifications to the method resulting from petition method validation.

OPPTS GLN 860.1360: Multiresidue Method

Glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate were not quantitatively recovered from any of the FDA Multiresidue Testing Protocols. This information has been forwarded to FDA (PP#8F3607, J. Garbus, 14-Aug-1988; PP#5F4578, M. Rodriguez, 10-Oct-1995).

OPPTS GLN 860.1380: Storage Stability Data

The petitioner submitted a storage stability study investigating the recovery of fortified residues of glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate in/on transgenic sugar beet tops and roots (MRID 44827901). The samples were fortified with 0.25 ppm of each compound and frozen until analysis. Stored samples and freshly fortified samples were analyzed using method BK/04/95. Results from the sugar beet storage stability study are presented in Table 8.

Table 8: Storage Stability in Transgenic Sugar Beet Tops and Roots

analyte [2]	fortification (ppm)	storage period (months)	freshly fortified % recovery [1]	apparent recovery in stored samples	corrected % recovery in stored samples
tops					
HOE 039866	0.25	3	60.8	75.6, 59.6	124, 98.0
		6	51.9	68.3, 71.5	132, 138
		12	68.8	64.8, 67.4	94.2, 98.0
		24	80.2	63.6, 64.2	79.3, 80.0

analyte [2]	fortification (ppm)	storage period (months)	freshly fortified % recovery [1]	apparent recovery in stored samples	corrected % recovery in stored samples
HOE 099730	0.25	3	85.8	76.0, 78.8	88.6, 91.8
		6	49.6	56.8, 59.8	115, 121
		12	70.0	80.7, 81.3	115, 116
		24	80.2	67.2, 76.8	83.8, 95.8
HOE 061517	0.25	3	94.8, 99.8	95.1, 87.8	97.7, 90.2
		6	96.6, 105	100, 102	99.2, 101
		12	96.9, 93.9	85.8, 97.5	89.9, 102
		24	118, 116	[illegible], 108	92.3, 92.3
roots					
HOE 039866	0.25	3	79.8, 94.5	81.1, 77.2	93.1, 88.6
		6	86.2	81.2, 88.4	94.2, 103
		12	108	104, 96.0	96.3, 88.9
		24	63.8	73.5, 85.3	115, 135
HOE 099730	0.25	3	87.0	81.7, 71.4	93.9, 82.1
		6	100	106, 105	106, 105
		12	98.5	103, 98.3	105, 99.8
		24	82.2	82.7, 87.2	101, 106
HOE 061517	0.25	3	97.4, 102, 91.6	91.9, 95.2	94.7, 98.1
		6	88.4, 100	107, 117	114, 124
		12	96.6, 85.6	107, 91.0	117, 99.9
		24	106, 115	111, 124	100,112

[1] average of freshly fortified samples used for calculation of % corrected recoveries

[2] HOE 039866 = glufosinate ammonium, HOE 099730 = N-acetyl glufosinate, HOE 061517 = 3-methylphosphinico propionic acid

Conclusions: The submitted storage stability study indicates that glufosiante ammonium, N-acetyl glufosinate and 3-methylphosphinico propionic acid are stable in transgenic sugar beet tops and roots for 24 months.

Previously submitted and reviewed storage stability data indicate that glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid are stable for 24 months in apples, corn grain and soybeans

(PP#8F3607, J. Garbus, 8-Aug-1990). Additional storage stability data indicate that glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate are stable for 12 months in transgenic soybean seed, forage and hay; for 3 months in soybean oil and meal; for 6 months in transgenic corn grain, fodder and forage; and for 3 months in eggs, liver, kidney and muscle (D211531 and D219069, M. Rodriguez, 7-Mar-1996).

OPPTS GLN 860.1480: Meat/Milk/Poultry/Eggs

Two dairy cow and two poultry feeding studies have been previously submitted, reviewed and determined to be adequate: **(1)** dairy cows and poultry feed a diet containing a 3:1 mixture of glufosinate ammonium and 3-methylphosphinico propionic acid (PP#8F3607, J. Garbus, 8-Aug-1990) and **(2)** dairy cows and poultry feed a diet containing 15% glufosinate ammonium and 85% N-acetyl glufosinate (D211531 & D211531, M. Rodriguez, 7-Mar-1996). Two feeding studies were performed on dairy cows and poultry due the different residues present in transgenic (principally N-acetyl glufosinate followed by glufosinate ammonium) and non-transgenic crops (principally 3-methylphosphinico propionic acid). Since the majority of the dietary burden to ruminants and poultry originates from transgenic crops, the feeding studies performed with N-acetyl glufosinate and glufosinate ammonium will be considered representative.

Considering all registered and proposed crops the maximum theoretical dietary burden is 14.55 ppm for beef cattle (aspirated grain fractions, corn field forage, cannery waste), 14.22 ppm for dairy cattle (aspirated grain fractions, corn field forage, cannery waste, molasses), 2.62 ppm for poultry (soybean hulls, soybean meal, soybean seed, canola meal) and 8.07 ppm for swine (aspirated grain fractions, canola meal, potato culls). Using these dietary burdens and the feeding studies performed with N-acetyl glufosinate and glufosinate ammonium, no adjustment in ruminant and,poultry tolerances are necessary.

Table 9: Commodity Contribution to Animal Dietary Burden

commodity	tolerance (ppm)	% dry matter	% diet				ppm in feed			
			beef	dairy	poultry	swine	beef	dairy	poultry	swine
previously registered commodities										
almond hulls	0.50	90	10	10	*	*	0.06	0.06	*	*
apple pomace	0.05	40	40	20	*	*	0.05	0.03	*	*
aspirated grain fractions	25.0	85	20	20	*	20	5.88	5.88	*	5.88
corn field grain	0.2	88	80	40	80	80	0.18	0.09	0.18	0.18
corn milled by products	0.2	85	50	25	60	75	0.12	0.06	0.14	0.18
[1]*corn forage*	4.0	40	40	50	*	*	4.00	5.00	*	*
[1]*corn stover*	6.0	83	25	15	*	*	1.81	1.08	*	*
[1]*cannery waste*	4.0	30	35	20	*	*	4.67	2.67	*	*
soybean hulls	5.0	90	20	20	20	*	1.11	1.11	1.11	*
soybean meal	2.0	92	15	15	40	25	0.33	0.33	0.87	0.54
soybean seed	2.0	89	15	15	20	25	0.34	0.34	0.45	0.56
soybean silage	2.0	30	30	30	*	*	2.00	2.00	*	*
commodities which are part of this petition										
sugar beet tops	1.5	23	20	10	*	*	1.30	0.65	*	*
sugar beat pulp	0.9	88	20	20	*	*	0.20	0.20	*	*
molasses	5.0	75	10	10	*	*	0.67	0.67	*	*
canola meal	1.1	88	15	15	15	15	0.19	0.19	0.19	0.19
potato culls	0.8	20	75	40	*	50	3.00	1.60	*	2.00
potato processed waste	0.8	15	75	40	*	*	4.00	2.13	*	*

– feeding restriction on soybean forage and hay therefore not include in calculation of dietary burdens
– *italicized commodities* originate from transgenic crops
[1] field or sweet corn forage and stover

OPPTS GLN 860.1500: Crop Field Trials

CANOLA

MRID 44358608: Determination of HOE 039866 Residues and its Metabolites HOE 061517 and HOE 085355 in Glufosinate Tolerant Canola (Brassica Napus) Generated from 1993 Field Trials: A total of 10 field trials were conducted during 1993 in Saskatchewan (n=3), Manitoba (n=3) and Alberta (n=4). Grain samples were harvested 57-83 days following a single broadcast spray application of glufosinate ammonium at 0.44 - 1.78 lbs ai/acre (0.6x - 2.3x the maximum proposed seasonal application rate). Applications were made at the 3-10 leaf stage in 12 gallons water/acre (timing of application at Westlock, Ab not recorded). A minimum of 500 grams of canola seed was collected after mechanical threshing and cleaning. Samples were frozen and shipped frozen to Xenos Laboratories Inc. (Ottawa, Ontario) where they were ground and kept frozen until residue analysis.

Samples were analyzed for residues of glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate using method HRAV-24 (essentially the same as AE-24, LOQ = 0.05 ppm). Apparent residues were less than the LOQ in/on all untreated samples. Residues in/on treated canola seed are summarized in Table 10. The petitioner indicated that the field portion of this study **was not** conducted according to GLP standards as specified in 40 CFR 160. Samples were stored for a maximum of 12 months prior to extraction and analysis (adequate transgenic soybean storage stability study covers this interval).

Table 10: Residues in/on Transgenic Canola Seed

location	lbs ai/acre	"x" proposed use rate	leaf stage[1]	PHI (days)	ppm[2]			
					039866	061517	085355	total
Innisfail, Ab	0.67	0.9	3-5	80	<0.05	<0.05	<0.05	<0.15
	1.34	1.8	3-5	80	<0.05	<0.05	<0.05	<0.15
	1.34	1.8	3-5	80	<0.05	<0.05	<0.05	<0.15
Westlock, Ab	0.45	0.6	*	75	<0.05	<0.05	<0.05	<0.15
	0.67	0.9	*	75	<0.05	<0.05	<0.05	<0.15
Fairview, Ab	0.45	0.6	4-5	75	<0.05	<0.05	<0.05	<0.15
	1.34	1.8	4-5	75	<0.05	<0.05	<0.05	<0.15
	1.34	1.8	4-5	75	<0.05	<0.05	<0.05	<0.15
Olds, Ab	0.45	0.6	3-5	83	<0.05	<0.05	<0.05	<0.15
	0.67	0.9	3-5	83	<0.05	<0.05	<0.05	<0.15
Brandon, Mb	0.67	0.9	4-6	69	0.122	<0.05	<0.05	<0.222
	0.67	0.9	4-6	69	0.106	<0.05	<0.05	<0.206
Rosebank, Mb	0.41	0.6	4-5	67	<0.05	<0.05	<0.05	<0.15

location	lbs ai/acre	"x" proposed use rate	leaf stage[1]	PHI (days)	ppm[2]			
					039866	061517	085355	total
	0.62	0.8	4-5	67	<0.05	<0.05	<0.05	<0.15
Souris, Mb	0.41	0.6	4-5	68	<0.05	<0.05	<0.05	<0.15
	0.62	0.8	4-5	68	<0.05	<0.05	<0.05	<0.15
Rosthern, Sk	0.94	1.3	5	66	<0.05	<0.05	0.053	<0.153
	1.82	2.5	5	66	<0.05	<0.05	0.098	<0.198
Lake Lenore, Sk	0.54	0.7	3-4	57	<0.05	<0.05	<0.05	<0.15
	0.84	1.2	3-4	57	<0.05	<0.05	<0.05	<0.15
Outlook, Sk	0.52	0.7	10	69	<0.05	<0.05	<0.05	<0.15
	0.8	1.1	10	69	<0.05	<0.05	<0.05	<0.15

1 leaf stage at application
2 concentrations expressed in terms of glufosinate free acid equivalents; HOE prefix eliminated; 039866 = glufosinate ammonium, 085355 = N-acetyl glufosinate, 061517 = 3-methylphosphinico propionic acid
* leaf stage at application not recorded

MRID 44358609: Determination of HOE 039866 Residue and its Metabolites HOE 085355 and HOE 061517 in Glufosinate Tolerant Canola (Brassica Napus) Generated from 1994 Field Trials: A total of 4 field trials were conducted during 1994 in Saskatchewan (n=1), Manitoba (n=2) and Alberta (n=1). Grain samples were harvested 57-77 days following a single broadcast spray application of glufosinate ammonium at 0.36, 0.71 or 1.07 lbs ai/acre (0.5x, 0.9x and 1.4x the maximum proposed seasonal application rate). Applications were made at the 1-3 leaf stage or 4-6 leaf stage in 12 gallons water/acre. A minimum of 500 grams of canola seed was collected after mechanical threshing and cleaning. Samples were frozen immediately and shipped frozen to Xenos Laboratories Inc. (Ottawa, Ontario) where they were ground and kept frozen until residue analysis.

Samples were analyzed for residues of glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate using method XAM-24 (essentially the same as AE-24, LOQ = 0.05 ppm). Apparent residues were less than the LOQ in/on all untreated samples. Residues in/on treated canola seed are summarized in Table 11. The petitioner indicated that this study was conducted according to GLP standards as specified in 40 CFR 160. Samples were stored for a maximum of 4 months prior to extraction and analysis (adequate transgenic soybean storage stability study covers this interval).

Table 11: Residues in/on Transgenic Canola Seed

location	lbs ai/acre	"x" proposed use rate	leaf stage[1]	PHI (days)	ppm[2]			
					039866	061517	085355	total
Indian Head, Sk	0.36	0.5	2-3	73	<0.05	<0.05	<0.05	<0.15
	0.71	1.0	2-3	73	<0.05	<0.05	<0.05	<0.15

location	lbs ai/acre	"x" proposed use rate	leaf stage[1]	PHI (days)	ppm[2]			
					039866	061517	085355	total
	1.07	1.5	2-3	73	<0.05	<0.05	<0.05	<0.15
	0.36	0.5	5-7	57	<0.05	<0.05	0.169	<0.269
	0.71	1.0	5-7	57	<0.05	<0.05	0.236	<0.336
	1.07	1.5	5-7	57	<0.05	<0.05	0.255	<0.355
Minto, Mb	0.36	0.5	2	77	<0.05	<0.05	<0.05	<0.15
	0.71	1.0	2	77	<0.05	<0.05	<0.05	<0.15
	1.07	1.5	2	77	<0.05	<0.05	<0.05	<0.15
	0.36	0.5	5-6	70	<0.05	<0.05	<0.05	<0.15
	0.71	1.0	5-6	70	<0.05	<0.05	<0.05	<0.15
	1.07	1.5	5-6	70	<0.05	<0.05	0.055	<0.155
Vauxhall, Ab	0.36	0.5	2-4	77	<0.05	<0.05	<0.05	<0.15
	0.71	1.0	2-4	77	<0.05	<0.05	<0.05	<0.15
	1.07	1.5	2-4	77	<0.05	<0.05	<0.05	<0.15
	0.36	0.5	4-6	67	<0.05	<0.05	0.081	<0.181
	0.71	1.0	4-6	67	<0.05	<0.05	0.171	<0.271
	1.07	1.5	4-6	67	0.053	<0.05	0.242	<0.345
Portage la Prairie, Mb	0.36	0.5	4-5	65	<0.05	<0.05	<0.05	<0.15
	0.71	1.0	4-5	65	<0.05	<0.05	0.066	<0.166
	1.07	1.5	4-5	65	<0.05	0.056	0.053	<0.159

1 leaf stage at application

2 concentrations expressed in terms of glufosinate free acid equivalents; HOE prefix eliminated; 039866 = glufosinate ammonium, 085355 = N-acetyl glufosinate, 061517 = 3-methylphosphinico propionic acid

Summary Canola: The petitioner has requested a canola seed tolerance of 0.4 ppm for the combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate. The petitioner indicated that only the spring variety of canola has been genetically modified for tolerance to glufosinate ammonium. In Region 2, canola is only planted in the winter months (winter variety of canola) due to the unfavorable climate for canola in the summer. Therefore, the petitioner is not requesting registration for application of glufosinate ammonium to transgenic canola in Region 2.

The petitioner submitted two field trial studies conducted in Canada (*MRID* 443586-08 & -09). The field portion of MRID 443586-08 was not conducted according to GLP standards. The deficiencies which lead to nonconformance were not provided. Information pertaining to the application date, method, equipment, volume, timing and rate were provided. Therefore, the factors that lead to nonconformance with GLP standards will be considered minor and the study is acceptable. The field trial data conducted as part of MRID 443586-09 is also acceptable.

The combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate in/on transgenic canola seed following a single application of glufosinate ammonium at 0.9x or 1.3x the maximum proposed seasonal use rate ranged from <0.15 - <0.336 ppm (treated at 3-7 leaf stage; PHI = 57 - 83 days).

According to Table 5 of OPPTS GLN 860.1500, a total of 8 trials conducted in Regions 2 (n=1, not necessary for this petition), 5 (n=2), 7 (n=2) and 11 (n=3) are suggested. The Canadian field trial data submitted with this petition can be applied to the following regions (HED SOP 98_2); Region 7 (n=2) and Region 14 (n=12; Region 14 is unique to Canada). The issue of how to apply canola field trial data from Region 14 to a US Registration was brought to Chem SAC. B. Schneider gathered information on canola production in the US and Canada and concluded that the majority of US canola is grown in ND, MN, MT, WA and SD. Generally within these states the northern most counties are the highest producing areas of the state. The canola production in Region 11 has decreased and increased in Regions 5 and 7 since the guidelines were written. The SAC agreed on accepting the Canadian canola field trials for glufosinate ammonium due to the similarities between the US canola production areas and Region 14 (Minutes of 17-Jun-1999 ChemSAC meeting). Geographical distribution of the submitted field trials is adequate for establishment of a tolerance in/on canola.

HED concludes that based on the submitted field trial data, the petitioners proposed tolerance of 0.4 ppm is appropriate. The Canadian MRL for the combined residues of glufosinate ammonium and 3-methylphosphinico propionic acid in/on canola is 3.0 ppm. In light of harmonization with Canada, the appropriate tolerance in/on canola seed for the combined residues of glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate expressed as glufosinate ammonium free acid equivalents, is 3.0 ppm.

SUGAR BEET

MRID 44358602: Magnitude of Glufosinate-Ammonium Residues In or On Trangenic Sugar Beets Resulting From Multiple Applications of Liberty™ Herbicide at Three Rates, USA, 1995: A total of 4 field trials were conducted during 1995 in California (n=1; Region 10), Idaho (n=1; Region 11), North Dakota (n=1; Region 5) and Minnesota (n=1; Region 5). One control and three treated plots were planted at each trial site. The first plot was treated three times at a nominal rate of 0.18 lbs ai/acre/application (0.4x the maximum single application rate), once at the 2-leaf stage, once at the 6-leaf stage and once at the 8-leaf stage (total treatment 0.54 lbs ai/acre; 0.6x the maximum seasonal application rate). The second plot was treated three times at a nominal rate of 0.36 lbs ai/acre/application (0.9x the maximum single application rate), at the same growth stages (total treatment 1.08 lbs ai/acre; 1.1x the maximum seasonal application rate). The third plot was treated two times at a nominal rate of 0.54 lbs ai/acre/application (1.3x the maximum single application rate), once at the 6-leaf stage and once at the 8-leaf stage (total treatment 1.08 lbs ai/acre; 1.1x the maximum seasonal application rate). All applications were made over the top with broadcast spray equipment in 10 gallons of water per acre. After collection, the tops plus the crown tissue were cut from the roots and packaged separately. All samples were frozen within 90 minutes of harvest and shipped frozen to the AgroEvo Research Center for homogenization. The homogenized samples were shipped frozen to Xenos laboratories (Ottawa, Ontario) where they were kept frozen until analysis.

Samples were analyzed for residues of glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate using method BK/04/95 (essentially the same as HRAV-5A, LOQ = 0.05 ppm). This method does not distinguish between glufosinate ammonium and N-acetyl glufosinate. Apparent residues were less than the LOQ in/on all untreated samples. Residues in/on treated sugar beet tops and roots are summarized in Table 12. The petitioner indicated that this study **was** conducted according to GLP standards as specified in 40 CFR 160 except for a few minor exceptions. Samples were stored for a maximum of 12 months prior to extraction and analysis (adequate storage stability study cover this interval).

Table 12: Residues in/on Transgenic Sugar Beet Tops and Roots

location	total applied (lbs ai/acre)	PHI[1] (days)	tops[2] (ppm)			roots[2] (ppm)		
			039866/ 099730	061517	total	039866/ 099730	061517	total
Fresno, CA	0.55[3]	10	0.19 0.23	<0.05 <0.05	<0.24 <0.28	–	–	–
		15	0.31 0.29	0.14 0.17	0.45 0.46	–	–	–
		30	0.23 0.28	0.53 0.54	0.76 0.82	–	–	–
		60	0.13 0.12	0.37 0.33	0.50 0.45	–	–	–
		139	<0.05 <0.05 <0.05	0.08 0.06 0.12	<0.13 <0.11 <0.17	<0.05 <0.05	0.14 0.14	<0.19 <0.19
	1.10[4]	10	0.39 0.46	<0.05 <0.05	<0.44 <0.51	–	–	–
		15	1.04 1.11 1.22	0.51 0.37 0.48	1.55 1.48 1.70	–	–	–
		30	0.63 0.76	1.20 1.07	1.83 1.83	–	–	–
		60	0.39 0.32	0.88 0.78	1.27 1.10	–	–	–
		139	<0.05 <0.05	0.21 0.25	<0.26 <0.30	<0.05 <0.05	0.30 0.32	<0.35 <0.37
	1.08[5]	10	3.01 3.55	0.25 0.22	3.26 3.77	–	–	–
		15	2.47 2.75 2.02	0.58 0.44 0.42	3.05 3.19 2.44	–	–	–

location	total applied (lbs ai/acre)	PHI[1] (days)	tops [2] (ppm)			roots [2] (ppm)		
			039866/ 099730	061517	total	039866/ 099730	061517	total
		30	1.15 1.25	1.17 1.40	2.32 2.65	–	–	–
		60	0.48 0.60 0.45	0.82 0.70 0.81	1.30 1.30 1.26	–	–	–
		139	0.05 0.08 <0.05	0.29 0.22 0.21	0.34 0.30 <0.26	<0.05 0.05	0.27 0.31	<0.32 0.36
Jerome, ID	0.56 [3]	41	0.08 0.09	<0.05 <0.05	<0.13 <0.14	0.06 <0.05 <0.05	<0.05 <0.05 <0.05	<0.11 <0.10 <0.10
	1.11 [4]	41	0.22 0.23	<0.05 <0.05	<0.27 <0.28	0.16 0.15	<0.05 <0.05	<0.21 <0.20
	1.10 [5]	41	0.31	0.05	0.36	0.21	0.06	0.27
Cass, ND	0.58 [3]	104	0.05 0.09 0.05	<0.05 <0.05 <0.05	<0.10 <0.14 <0.10	0.08 0.06 0.08	<0.05 <0.05 <0.05	<0.13 <0.11 <0.13
	1.17 [4]	104	0.11 0.07 0.11	<0.05 <0.05 <0.05	<0.16 <0.12 <0.16	0.14 0.15	<0.05 <0.05	<0.19 <0.20
	1.34 [5]	104	0.07 0.08	<0.05 <0.05	<0.12 <0.13	0.15 0.12	<0.05 <0.05	<0.20 <0.17
Polk, MN	0.53 [3]	95	<0.05 <0.05	<0.05 <0.05	<0.10 <0.10	<0.05 <0.05	<0.05 <0.05	<0.10 <0.10
	1.10 [4]	95	<0.05 <0.05	<0.05 <0.05	<0.10 <0.10	0.09 0.09	<0.05 <0.05	<0.14 <0.14
	1.09 [5]	95	0.10 0.09	<0.05 <0.05	<0.15 <0.14	0.12 0.10	<0.05 <0.05	<0.17 <0.15

1 California samples collected at the following plant stages, 10 day PHI = 12-13 leaf stage, 15 day PHI = 13 leaf stage, 30 day PHI = 16-18 leaf stage, 60 day PHI = vegetative, 139 day PHI = mature; Idaho 41 day PHI = immature; North Dakota 104 day PHI = mature; Minnesota 95 day PHI = mature

2 concentrations expressed in terms of glufosinate free acid equivalents; HOE prefix eliminated; 039866 = glufosinate ammonium, 099730 = N-acetyl glufosinate, 061517 = 3-methylphosphinico propionic acid

3 three applications at a nominal rate of 0.18 lbs ai/acre, once at the 2-leaf stage, once at the 6-leaf stage and once at the 8-leaf stage (total treatment 0.54 lbs ai/acre, 0.6x maximum seasonal application rate)

4 three applications at a nominal rate of 0.36 lbs ai/acre at the same growth stages as "1" (total treatment 1.08 lbs ai/acre, 1.1x maximum seasonal application rate)

5 two applications at a nominal rate of 0.54 lbs ai/acre, once at the 6-leaf stage and once at the 8-leaf stage (total treatment 1.08 lbs ai/acre, 1.1x maximum seasonal application rate)

MRID 44358603: Magnitude of Glufosinate-Ammonium Residues In or On Transgenic Sugar Beet Raw Agricultural Commodities Resulting From Multiple Applications of Liberty™ Herbicide at Two Rates, USA, 1996: A total of 10 field trials were conducted during 1995 in Michigan (n=1; Region 5), Ohio (n=1; Region 5), North Dakota (n=2; Regions 5 and 7), Nebraska (n=1; Region 7), Colorado (n=2; Regions 8 and 9), California (n=1; Region 10) and Idaho (n=2; both in Region 11). One control and two treated plots were planted at each trial site. The first plot was treated two times at a nominal rate of 0.54 lbs ai/acre/application (1.1x the maximum single application rate), once at the 6-leaf stage and once at the 8-leaf stage (total treatment 1.08 lbs ai/acre; 1.1x maximum seasonal application rate). The second plot was treated at a nominal rate of 0.54 lbs ai/acre (1.1x the maximum single application rate) at the 2-leaf stage, and then treated at a nominal rate of 0.35 lbs ai/acre (0.7x the maximum single application rate) at the 6-leaf stage and finally once at a nominal rate of 0.54 lbs ai/acre (1.1x the maximum single application rate) at the 10-leaf stage (total treatment 1.44 lbs ai/acre; 1.5x maximum seasonal application rate). All applications were made over the top with broadcast spray equipment in 10 gallons of water per acre. The sugar beets from each plot were harvested at maturity. After collection, the tops plus the crown tissue were cut from the roots and packaged separately. All samples were frozen within 2 hours of harvest and shipped frozen to the AgroEvo Research Center for homogenization. The homogenized samples were shipped frozen to Xenos laboratories (Ottawa, Ontario) where they were kept frozen until analysis.

Samples were analyzed for residues of glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate using method BK/04/95 (essentially the same as HRAV-5A, LOQ = 0.05 ppm). This method does not distinguish between glufosinate ammonium and N-acetyl glufosinate. Apparent residues were less than the LOQ in/on all untreated samples. Residues in/on treated sugar beet tops and roots are summarized in Table 13. The petitioner indicated that this study was conducted according to GLP standards as specified in 40 CFR 160 except for a few minor exemptions. Samples were stored for a maximum of 6 months prior to extraction and analysis (adequate storage stability studies cover this interval). The trial conducted in Canyon, ID was canceled (no explanation was given).

Table 13: Residues in/on Transgenic Sugar Beet Tops and Roots

location	total applied (lbs ai/acre)	PHI (days)	tops [1] (ppm)			roots [1] (ppm)		
			039866/ 099730	061517	total	039866/ 099730	061517	total
Ottawa, MI	1.08	109	0.143 0.163	<0.05 0.051	<0.148 0.214	0.122 0.128	0.053 0.059	0.175 0.187
	1.43	109	0.295 0.297	<0.05 <0.05	<0.300 <0.302	0.239 0.212	0.050 <0.05	0.289 <0.262
Fayette, OH	1.08	83	0.159 0.157	<0.05 <0.05	<0.164 <0.162	0.273 0.119	<0.05 <0.05	<0.323 <0.169
	1.43	77	0.459 0.461	<0.05 <0.05	<0.464 <0.466	0.558 0.780	<0.05 <0.05	<0.608 <0.830 **HAFT = 0.719**
Cass, ND	1.08	67	0.251 0.241	<0.05 <0.05	<0.256 <0.246	0.172 0.163	<0.05 <0.05	<0.222 <0.213

location	total applied (lbs ai/acre)	PHI (days)	tops[1] (ppm)			roots[1] (ppm)		
			039866/ 099730	061517	total	039866/ 099730	061517	total
	1.43	62	0.645 0.530	<0.05 <0.05	<0.649 <0.535	0.535 0.695	<0.05 <0.05	<0.585 <0.745
Scotts Bluff, NB	1.08	115	<0.05 <0.05	<0.05 <0.05	<0.10 <0.10	<0.05 <0.05	<0.05 <0.05	<0.10 <0.10
	1.43	108	<0.05 <0.05	<0.05 <0.05	<0.10 <0.10	0.073, 0.054	<0.05 <0.05	<0.123 <0.104
Ward, ND	1.08	73	0.129 0.156	<0.05 <0.05	<0.134 <0.161	0.118 0.137	<0.05 <0.05	<0.168 <0.187
	1.43	66	0.230 0.235	0.057 0.076	0.287 0.311	0.280 0.326	0.072 0.113	0.352 0.439
Weld, CO	1.08	80	<0.05 <0.05	<0.05 <0.05	<0.10 <0.10	<0.05 <0.05	<0.05 <0.05	<0.10 <0.10
	1.43	68	0.376 0.383	<0.05 <0.05	<0.381 <0.388	0.526 0.549	<0.05 <0.05	<0.576 <0.599
Weld, CO	1.08	86	0.061 0.056	<0.05 <0.05	<0.111 <0.106	0.106 0.112	<0.05 <0.05	<0.156 <0.162
	1.43	81	0.221 0.238	<0.05 <0.05	<0.226 <0.243	0.273 0.304	<0.05 <0.05	<0.323 <0.354
Fresno, CA	1.08	132	<0.05 0.065	<0.05 <0.05	<0.10 <0.10	0.059 0.084	0.065 0.058	0.124 0.142
	1.43	122	0.185 0.260	0.057 0.075	0.242 0.335	0.371 0.357	0.055 0.066	0.426 0.423
Jerome, ID	1.08	128	0.106 0.067	<0.05 <0.05	<0.156 <0.117	0.072 0.063	<0.05 <0.05	<0.122 <0.113
	1.43	121	0.315 0.298	0.058 0.052	0.373 0.350	0.189 0.216	<0.05 <0.05	<0.239 <0.266

HAFT = highest average field trial

[1] concentrations expressed in terms of glufosinate free acid equivalents; HOE prefix eliminated; 039866 glufosinate ammonium, 099730 = N-acetyl glufosinate, 061517 = 3-methylphosphinico propionic acid

Summary Sugar Beet: The petitioner has requested a sugar beet top tolerance of 1.3 ppm and a sugar beet root tolerance of 0.7 ppm for the combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate expressed as glufosinate free acid equivalents.

The two submitted sugar beet field trial studies are adequate (MRIDs 443586-02 and -03). The combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate in/on transgenic sugar beet tops and roots treated with Liberty™ Herbicide at 1.1x - 1.5x the maximum proposed seasonal use rate ranged from <0.10 -1.30 ppm (tops) and <0.10 - <0.830 ppm (roots). Pre-harvest intervals ranged from 41 - 139 days. Only 4 of the 14 field trials had a pre-harvest interval less than 80 days (label specifies a PHI = 60 days). The label indicates that the product may be applied from the cotyledon to 10 leaf stage of the sugar beet. The final application for all field trials was either at the 8 or 10 leaf stage and samples were harvested when the crop reached maturity. Since crop harvest was governed by crop development and the increased PHIs were counteracted in some cases by application rates 1.5x the maximum proposed rate, HED concludes that the field trial data is acceptable. Geographical distribution of the submitted field trials is adequate for establishment of a tolerance in/on sugar beets.

HED concludes that based on the submitted field trial data, the appropriate tolerance in/on sugar beet tops and roots, as result of the application of glufosinate ammonium as defined in this petition, is 1.5 ppm and 0.9 ppm, respectively. The petitioner must submit a revised Section F proposing a 1.5 ppm tolerance in/on sugar beet tops and a 0.9 ppm tolerance in/on sugar beet roots for the combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate expressed as glufosinate free acid equivalents.

POTATO

MRID 44583901: Magnitude of Glufosinate-Ammonium In or On Potatoes Resulting From a Single Application of Rely® Herbicide, USA 1997: A total of 20 field trials were conducted during 1995 in New York (n=1; Region 1), Pennsylvania (n=2; both in Region 1), New Jersey (n=2; both in Region 2), Florida (n=2; both in Region 3), Illinois (n=1; Region 5), Minnesota (n=1; Region 5), Iowa (n=1; Region 5), North Dakota (n=1; Region 5), Utah (n=2; both in Region 9), California (n=1; Region 10) and Idaho (n=6; all in Region 11). One control and one treated plot were planted at each trial site. The treated plot received a single application of glufosinate-ammonium at 0.40 lbs ai/acre (1.1x the maximum proposed seasonal application rate) 5-7 days after plant senescence began. All applications were made over the top with broadcast spray equipment in 10 gallons of water per acre. Samples were harvested by hand 9-10 days after treatment. All samples were transferred to a freezer within 5 hours of harvest and shipped frozen to the AgroEvo Research Center (Pikeville, NC) for homogenization. The homogenized samples were shipped frozen to Xenos laboratories (Ottawa, Ontario) where they were kept frozen until analysis.

Samples were analyzed for residues of glufosinate ammonium and 3-methylphosphinico propionic acid using method BK/05/95 (LOQ = 0.05 ppm). This method is a modification of HRAV-5A (the anion exchange cleanup step is eliminated). Apparent residues were less than the LOQ in/on all untreated samples. Residues in/on treated potatoes are summarized in Table 14. The petitioner indicated that this study was conducted according to GLP standards as specified in 40 CFR 160 except for a few minor exceptions. Samples were stored for a maximum of 7 months prior to extraction and analysis (adequate transgenic sugar beet storage stability study covers this interval).

Table 14: Residues in/on Potatoes

location	ppm [1]		
	HOE 039866	HOE 061517	total
Wayne, NY	<0.05, <0.05	<0.05, <0.05	<0.10, <0.10
Lehigh, PA	0.288, 0.277	<0.05, <0.05	<0.338, <0.327

location	ppm[1]		
	HOE 039866	HOE 061517	total
Berks, PA	0.098, 0.125	<0.05, <0.05	<0.148, <0.175
Salem, NJ	0.072, 0.117	<0.05, <0.05	<0.122, <0.167
Middlesex, NJ	0.136, 0.146	<0.05, <0.05	<0.186, <0.196
Collier, FL	0.369, 0.276	<0.05, <0.05	<0.419, <0.326
Lee, FL	0.607, 0.617	<0.05, <0.05	<0.657, <0.667 **HAFT = 0.662**
Clinton, IL	0.055, <0.05	<0.05, <0.05	<0.105, <0.10
Freeborn, MN	0.434, 0.329	<0.05, <0.05	<0.484, <0.379
Gerro Gordo, IA	0.190, 0.162	<0.05, <0.05	<0.240, <0.212
Grand Forks, ND	<0.05, <0.05	<0.05, <0.05	<0.10, <0.10
Cache, UT	0.246, 0.240	<0.05, <0.05	<0.296, <0.290
Box Elder, UT	<0.05, <0.05	<0.05, <0.05	<0.10, <0.10
Tulare, CA	<0.05, <0.05	<0.05, <0.05	<0.10, <0.10
Franklin, ID	0.130, 0.120	<0.05, <0.05	<0.180, <0.170
Power, ID	0.247, 0.262	<0.05, <0.05	<0.297, <0.312
Bingham, ID	0.132, 0.094	<0.05, <0.05	<0.182, <0.144
Cassia, ID	0.117, 0.132	<0.05, <0.05	<0.167, <0.182
Bannock, ID	<0.05, 0.073	<0.05, <0.05	<0.10, <0.10
Bonneville, ID	0.160, 0.159	<0.05, <0.05	<0.210, <0.209

HAFT = highest average field trial
[1] concentrations expressed in terms of glufosinate free acid equivalents; HOE 039866 = glufosinate ammonium, HOE 061517 = 3-methylphosphinico propionic acid

Summary, Potatoes: The petitioner has requested a potato tolerance of 0.4 ppm for the combined residues of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents.

The submitted potato field trial study is adequate (MRID 44583901). The combined residues of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid in/on potatoes treated with Rely® Herbicide at 1.1x the maximum proposed seasonal use rate (PHI = 9-10 days) ranged from <0.10 - <0.667 ppm. Geographical distribution of the submitted field trials is adequate for establishment of a tolerance in/on potatoes.

HED concludes that based on the submitted field trial data, the appropriate tolerance in/on potatoes, as result of the application of glufosinate ammonium as defined in this petition, is 0.8 ppm. The petitioner must submit a revised Section F proposing a 0.8 ppm tolerance in/on potatoes for the combined residues of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents.

OPPTS GLN 860.1520: Processed Food/Feed

CANOLA

MRID 44358610: Determination of HOE 039866 Residues and its Metabolites HOE 085355 and HOE 061517 in Processed Fractions of Transgenic Canola Seed Treated with Glufosinate-Ammonium: A single field trial was conducted at Indian Head, Saskatchewan. Four plots were established, an untreated control and three plots treated at the 4-6 leaf stage with a single application of glufosinate ammonium at 0.67 lbs ai/acre (0.9x the maximum seasonal rate), 1.3 lbs ai/acre (1.8x the maximum seasonal rate) or 3.3 lbs ai/acre (4.5x the maximum seasonal rate). All applications were made with broadcast spray equipment in ~12 gallons of water per acre. Grain samples were collected 70 days after application. After mechanical thrashing and cleaning, all grain samples were transferred to a freezer. Approximately 5 kg of seed from each treatment were shipped to the Food Protein Research and Development Center, Texas A&M University (College Station, Texas) for processing.

Upon receipt to the processing facility the canola samples were dried and cleaned. Following conditioning, the majority of the crude oil was obtained by pressing in an expeller. The residual crude oil remaining in the presscake was extracted with hexane. A portion of the solvent-extracted meal was desolventized and toasted. The crude oil from the press and the extraction were combined and refined. The refined oil was bleached and deodorized. All samples were kept frozen and shipped frozen to Xenos Laboratories (Ottawa, Ontario) for analysis.

Samples were analyzed for residues of glufosinate ammonium, N-acetyl glufosinate and 3-methylphosphinico propionic acid using method HRAV-24 (similar to method AE-24, LOQ = 0.05 ppm). Apparent residues were less than the LOQ in/on all untreated samples. Residues in/on treated canola seed and processed commodities are summarized in Table 15. The petitioner indicated that this study was conducted according to GLP standards as specified in 40 CFR 160 except for a few minor exceptions.

Unprocessed canola seed was stored for a maximum of 7 months prior to extraction and analysis (adequate transgenic soybean storage stability study covers this interval). Canola seed samples were stored 4.5 months prior to processing into canola meal, oil and soapstock. The processed samples were stored for 4 months prior to analysis. Storage stability studies performed on transgenic soybean processed commodities demonstrated that all residue components were stable for 3 months. The storage intervals for the canola processed commodities are acceptable.

Table 15: Concentration/Reduction Factors for Canola Processed Commodities

commodity	ppm [1]				reduction/concentration factors [2]			
	HOE 039866	HOE 061517	HOE 099730	total	HOE 039866	HOE 061517	HOE 099730	total
0.67 lbs ai/acre								
seed	<0.05	<0.05	0.063	<0.163	--	--	--	--
untoasted	<0.05	<0.05	0.170	<0.270	--	--	2.7	1.9
toasted meal	<0.05	<0.05	0.206	<0.306	--	--	3.3	2.3
oil [3]	<0.05	<0.05	<0.05	<0.15	--	--	0.4	0.7
soapstock	<0.05	<0.05	<0.05	<0.15	--	--	0.4	0.7
1.3 lbs ai/acre								
seed	<0.05	<0.05	0.060	<0.160	--	--	--	--
untoasted	<0.05	<0.05	0.222	<0.322	--	--	3.7	2.5
toasted meal	<0.05	0.054	0.292	<0.396	--	2.2	4.9	3.4
oil [3]	<0.05	<0.05	<0.05	<0.15	--	--	0.4	0.7
soapstock	<0.05	<0.05	<0.05	<0.15	--	--	0.4	0.7
3.3 lbs ai/acre								
seed	<0.05	<0.05	0.211	<0.311	--	--	--	--
untoasted	<0.05	0.108 [4]	0.604 [4]	<0.762	--	4.3	2.9	2.8
toasted meal	<0.05	0.105	0.638	<0.793	--	4.2	3.0	2.9
oil [3]	<0.05	<0.05	<0.05	<0.15	--	--	0.1	0.3
soapstock	<0.05	<0.05	0.083	<0.183	--	--	0.4	0.5

1 concentrations expressed in terms of glufosinate free acid equivalents; HOE 039866 = glufosinate ammonium, HOE 099730 = N-acetyl glufosinate, HOE 061517 = 3-methylphosphinico propionic acid
2 residues <0.05 ppm were placed at ½ LOQ (0.025 ppm) for determination of reduction/concentration factors
3 residues in crude oil, refined oil, refined bleached oil and refined bleached deodorized oil were <0.05 ppm
4 average of replicate analysis

Summary Canola Processing Studies: The petitioner has requested a canola meal tolerance of 2.0 ppm for the combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate expressed as glufosinate free acid equivalents.

The submitted canola processing study is adequate (MRID 44358610). Canola seed harvested 70 days after treatment with glufosinate ammonium at 0.67, 1.3 or 3.3 lbs ai/acre/application (0.9x, 1.7x and 4.3x the maximum seasonal application rates; treated at 4-6 leaf stage) was processed into meal, oil and soapstock. The combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate did not concentrate in oil or soapstock but did concentrate 3.4x and 2.9x in toasted meal (average 3.2x). Since both metabolites were detected in toasted meal from the two highest treatment groups, only concentration factors from these groups were considered.

The highest field trial for canola seed was <0.336 ppm (Indian Head, Sk; MRID 44358609). The maximum combined glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate residue expected in/on transgenic canola meal, based on the highest field trial and the 3.2x concentration factor, is 1.1 ppm.

HED concludes that the appropriate tolerance in/on canola meal, as a result of the application of glufosinate ammonium to canola as defined in this petition, is 1.1 ppm. The petitioner must submit a revised Section F proposing a canola meal tolerance of 1.1 ppm for the combined residues of glufosinate ammonium and its metabolites N-acetyl glufosinate ammonium and 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents.

SUGAR BEET

MRID 44358604: Magnitude of Glufosinate-Ammonium Residues In or On Transgenic Sugar Beet Roots and Processed Commodities Resulting from Multiple Applications of Liberty™ Herbicide, USA, 1996: A single field trial was conducted at Fresno, California. Two plots were established, a untreated control and a treated plot which received three applications (2-leaf stage, 6-leaf stage and 8-leaf stage) of glufosinate ammonium at 2.5 - 2.7 lbs ai/acre/application (total applied 7.9 lbs ai/acre; 8.3x the maximum proposed seasonal application rate). All applications were made with broadcast spray equipment in ~10 gallons of water per acre. The sugar beet plants were allowed to grow to maturity and harvested by hand 136 days after the final application. Samples were transferred to a freezer within 10 minutes of collection. Samples were shipped frozen to Wm. J. Engler Associates, Inc. (Moses Lake, Washington) for processing into dried pulp, molasses and refined sugar.

The sugar beets were removed from frozen storage and a representative RAC was collected as an unprocessed sample. The sugar beets were washed and cut into slabs. Sugar was extracted in a series of steam heated cells with a mixture of fresh water and pulp press water. Extracted beet pulp was pressed to recover the sugar solution carried out with the pulp. The pressed pulp was dried to 1.7% moisture, milled and collected. The raw juice was purified in a stem jacketed kettle by addition of lime and carbon dioxide. The precipitate was allowed to settle and clarified juice was decanted and screened. The settled sludge was vacuum filtered and the filtrate combined with the decanted liquid. The clarified juice was further purified by a second carbonation with carbon dioxide gas and then vacuum filtered, concentrated and placed in frozen storage for later processing. The juice was thawed and filtered. The filtered thick juice was fed to a Laboratory Vacuum Pan and Granulator. The massecuite (mixture of sugar crystals and syrup) was centrifuged in a perforated bronze basket. The spun off syrup (molasses) was collected. Sugar retained in the basket was washed, dried and collected. Samples of the whole beet and processed commodities were shipped frozen to the ARC where the whole beets were homogenized. All samples were shipped frozen to Xenos Laboratories (Ottawa, Ontario) where they remained frozen until analysis.

Samples were analyzed for residues of glufosinate ammonium, N-acetyl glufosinate and 3-methylphosphinico propionic acid using method BK/04/95 (method is similar to HRAV-5A, LOQ = 0.05 ppm all sugar beet matrices). This method does not distinguish between glufosinate ammonium and N-acetyl glufosinate. Apparent residues were less than the LOQ in/on all untreated samples. Residues in/on treated sugar beet and processed commodities are summarized in Table 16. The petitioner indicated that this study was conducted according to GLP standards as specified in 40 CFR except for a few minor exceptions.

Unprocessed sugar beet samples were stored for a maximum of 5 months prior to extraction and analysis (an adequate sugar beet storage stability study cover this interval). Sugar beet samples were stored 2 months prior to processing into pulp, molasses and sugar. The processed samples were stored for 3 months prior to analysis. No storage stability data for sugar beet pulp, molasses or sugar have been submitted.

Table 16: Concentration/Reduction Factors for Sugar Beet Processed Commodities

commodity	ppm [1]			reduction/concentration factors [2]		
	HOE 039866/099730	HOE 061517	total	HOE 039866/099730	HOE 061517	total
Roots	0.228	0.929	1.157	--	--	--
Dried Pulp	0.141	0.585	0.726	0.6	0.6	0.6
Molasses	1.58	6.33	7.91	6.9	6.8	6.8
Refined Sugar	<0.05	<0.05	<0.10	0.1	<0.1	<0.1

1 concentrations expressed in terms of glufosinate free acid equivalents; HOE 039866 = glufosinate ammonium, HOE 099730 = N-acetyl glufosinate, HOE 061517 = 3-*methylphosphinico propionic acid*

2 residues <0.05 ppm were placed at ½ LOQ (0.025 ppm) for determination of reduction/concentration factors

Summary Sugar Beet Processing Study: The petitioner has requested a sugar beet molasses tolerance of 5.0 ppm for the combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate expressed as glufosinate free acid equivalents.

Sugar beets treated three times with Liberty™ Herbicide (2-leaf stage, 6-leaf stage and 8-leaf stage) at 2.5 - 2.7 lbs ai/acre/application (total applied 7.9 lbs ai/acre; 8.3x the maximum proposed seasonal application rate) were harvested 136 days after the final treatment and processed into pulp, molasses and sugar. The combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate did not concentrate in pulp or sugar but did concentrate 6.8x in molasses. Unprocessed sugar beet samples were stored for 5 months prior to analysis (adequate storage stability study covers this interval). Processed samples were stored for 3 months prior to analysis. No storage stability data for sugar beet pulp, molasses or sugar have been submitted.

The highest average field trial (HAFT) for sugar beet roots was 0.719 ppm (Fayette, OH; MRID 44358603). The maximum combined glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate residue expected in sugar beet molasses, based on the HAFT and the 6.8x concentration factor, is 5.0 ppm.

HED will not be opposed to conditional registration of glufosinate ammonium on transgenic sugar beets. Unconditional registration may be granted upon validation of the three month storage interval for the processed commodities (sugar, pulp and molasses). Pending submission and evaluation of this data, HED concludes that the petitioners proposed sugar beet molasses tolerance of 5.0 ppm, is appropriate.

POTATO

MRID 44358612: Glufosinate-Ammonium Derived Residues in Potatoes and Processed Commodities Following Vine Desiccation with Ignite at the Minimum Recommended PHI - USA, 1996: A single field trial was conducted at Ephrata, Washington. Two plots were established, an untreated control and a treated plot which received a single application of glufosinate ammonium at 2.0 lbs ai/acre (5.3x the maximum single and seasonal application rate). All applications were made with broadcast spray equipment in ~12 gallons of water per acre. Potatoes were harvested 9 days after application using a single row mechanical digger. The samples were shipped frozen to Xenos Laboratories (Ottawa, Ontario) and fresh to Wm. J. Engler and Associates, Inc. (Moses Lake, Washington) for processing into chips, flakes and wet peel.

Potato Chip Processing: Potatoes were washed, peeled and cut into ~0.16cm slices. The sliced potatoes were placed in warm water to remove free starch. The slices were drained over a screen to remove excess water and were fried in oil at ~180° C for 90 seconds. The fried potatoes were drained and salted. A sample of the potato chips was collected and placed in the freezer.

Potato Flake Processing: Potatoes were washed and batch steamed for 45 seconds (6.0 kg/cm^2). The steamed potatoes were scrubbed for 30 seconds and the potato peel collected. The collected peel was hydraulically pressed and combined with the cut trim waste and placed in the freezer. The peeled potatoes were cut into ~1.3 cm slabs and sprayed washed to remove free starch. The potato slabs were precooked at ~74° C for 20 minutes and cooled. The cooled potato slabs were steam cooked at ~100° C for 40 minutes, mashed and mixed with an emulsion of food additives. The wet mash was placed in a Overton Single Drum Dryer to dry the wet mash into a thin sheet. The dried potato mash was broken into large flakes by hand and placed on a fluidized bed dryer 3-5 minutes to complete the drying process. The flakes were feed into a hammermil for uniform milling of the finished potato flakes. A sample of the flakes was collected and frozen.

Samples of unprocessed potatoes, potato chips, potato flakes and wet peel were shipped frozen to Xenos Laboratories for analysis. Samples were analyzed for residues of glufosinate ammonium and its metabolite, 3-methylphosphinico propionic acid, using method XAM-24B (LOQ = 0.05 ppm, method is similar to HRAV-5A). Residues in/on treated potatoes and processed commodities are summarized in Table 17. The petitioner indicated that this study **was** conducted according to GLP standards as specified in 40 CFR except for a few minor exemptions.

Potato samples were processed within two days of collection. Processed and unprocessed potato samples were stored for a maximum of 3 months prior to extraction and analysis. Since processed potato commodities are not substantially different from the unprocessed commodity, the validated storage interval for transgenic sugar beet root samples of 24 months will be considered applicable to both processed and unprocessed potato commodities. The storage intervals for this study are within predetermined limits.

Table 17: Concentration/Reduction Factors for Potato Processed Commodities

commodity	ppm [1]			reduction/concentration factors [2]		
	HOE 039866	HOE 061517	total	HOE 039866	HOE 061517	total
potato	0.641	<0.05	<0.691	--	--	--
potato chips	1.49	<0.05	<1.54	2.3	--	2.3
potato flakes	1.96	<0.05	<2.01	3.1	--	3.0
potato wet peel	0.358	<0.05	<0.408	0.6	--	0.6

[1] concentrations expressed in terms of glufosinate free acid equivalents; HOE 039866 = glufosinate ammonium, HOE 061517 = 3-methylphosphinico propionic acid

[2] residues <0.05 ppm were placed at ½ LOQ (0.025 ppm) for determination of reduction/concentration factors

Summary Potato Processing Study: The petitioner has requested a potato flake tolerance of 1.3 ppm and a processed potato tolerance of 1.0 ppm for the combined residues of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents.

The submitted potato processing study is adequate (MRID 44358612). Potatoes harvested 9 days after a single treatment with glufosinate ammonium at 2.0 lbs ai/acre (5.3x the maximum proposed single and seasonal application rate) were processed into chips, flakes and peel. Glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid did not concentrate in potato peel but did concentrate 2.3x in potato chips and 3.0x in potato flakes.

The HAFT for potatoes was 0.662 ppm (Lee, FL; MRID 44583901). The maximum combined glufosinate ammonium and 3-methylphosphinico propionic acid residue expected in potato flakes, based on the HAFT and the 3.0x concentration factor, is 2.0 ppm. The maximum combined glufosinate ammonium and 3-methylphosphinico propionic acid residue expected in potato chips, based on the HAFT and the 2.3x concentration factor, is 1.6 ppm.

HED concludes that the appropriate tolerance in/on potato chips and potato granuales/flakes, as a result of the application of glufosinate ammonium to potatoes as defined in this petition, is 1.6 ppm and 2.0 ppm, respectively. The petitioner must submit a revised Section F proposing a potato chip tolerance of 1.6 ppm and a potato granule/flake tolerance of 2.0 ppm for the combined residues of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents.

OPPTS GLN 860.1850 & 860.1900: Confined/Field Accumulation in Rotational Crops

A confined accumulation in rotational crops study has been submitted, reviewed and determined to be adequate (MRID 43766917). Lettuce, radish and spring wheat were planted 28 and 119 days after the soil was treated with glufosinate ammonium at 0.9 lbs ai/acre (MRID 43766917). Based on the levels of extractable residues observed at the 119 day plantback interval, no additional data on rotational crops are required provided a 120 day plant back interval for all crops is placed on the label (D211531 and D219069, M. Rodriquez, 7-Mar-1996). A field rotational crop study performed with winter wheat has been submitted and reviewed (MRID 44432601). Winter wheat was planted 73 - 90 days after the soil was treated with glufosinate ammonium at 0.8 lbs ai/acre. Reported residues on/on treated samples of wheat forage, hay, straw and grain were less than the LOQ (LOQ = 0.05 ppm) (P. Errico [RD], 6-May-1998).

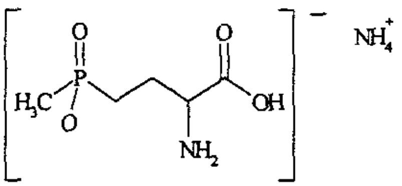
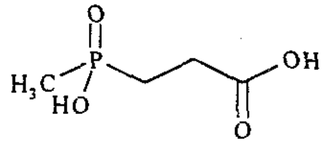
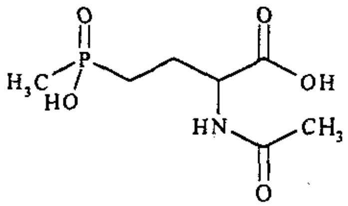
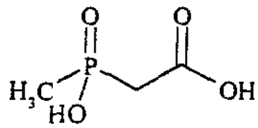
Conclusions: The submitted label indicates a 120 day plant back interval for wheat only. The label should be amended to indicate a 120 day plant back interval for all crops except wheat where a 70 day plant back interval is appropriate.

OPPTS GLN 860.1900: Field Accumulation in Rotational Crops

-no data submitted

cc: PP 7F04910 & 8F04997, T. Bloem (RAB1)
RDI: M. Morrow (9-Jul-1999), G. Kramer (8-Jul-1999), RAB1 Chemists (20-May-1999)
T. Bloem:806R:CM#2:(703)-605-0217

Attachment 1: Structure of glufosinate-ammonium and its metabolites in potato, transgenic canola and transgenic sugar beet commodities.

Common Name Chemical Name	Structure
glufosinate-ammonium ammonium-DL-homoalanin-4-yl(methyl) phosphinate (HOE 039866)	
3-methylphosphinico propionic acid (HOE 061517)	
N-acetyl-glufosinate 2-acetamido-4-methylphosphinico-butanoic acid (HOE 099730 or HOE 085355) (found only in transgenic crops)	
2-methylphosphinico-acetic acid	

013728

Attachment 4: Amendment of 5-August-1999

D258420, T. Bloem, 19-August-1999

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

19-August-1999

Memorandum

Subject: PP#s 7F04910, 8F04997 - AgrEvo USA Company has Requested a Section 3 Registration for use of Glufosinate Ammonium (Liberty™ and Rely®) on Potatoes, Transgenic Sugar Beets and Transgenic Canola. **Amendment of 5-August-1999.** DB Barcodes D258420. Chemical # 128850. Case #s 289177, 290273. Submission #s S529287, S545114

From: Tom Bloem, Chemist
RAB1/HED (7509C)

Through: Melba Morrow, DVM, Branch Senior Scientist
George Kramer, Ph.D., Chemist
RAB1/HED (7509C)

To: Joanne Miller/Eugene Wilson (PM Team 23)
RD (7505C)

AgrEvo USA Company has requested a Section 3 registration for use of glufosinate ammonium on potatoes, transgenic sugar beets and transgenic canola. Information submitted by the petitioner pertaining to residue chemistry data requirements were evaluated and several deficiencies noted (D257629, D257628, T. Bloem, 9-Jul-1999). The current amendment is HED's review of information submitted by the petitioner addressing these deficiencies.

Executive Summary of Chemistry Deficiencies

- Revised Section B (conclusion 1b)
- Storage stability Study for Sugar Beet Processed Commodities (sugar, pulp and molasses; 3 months)
- Successful Petition Method Validation for Methods BK/04/95 (sugar beets) and HRAV-24 (canola)

RECOMMENDATIONS

There are no residue chemistry data requirements that would preclude a conditional registration of glufosinate ammonium on transgenic sugar beets, transgenic canola and potatoes. Unconditional registration may be granted upon submission and evaluation of the information specified in conclusions 1b, 2 and 4. HED concludes that the following tolerances, for the combined residues of glufosinate ammonium, N-acetyl glufosinate and 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents, are appropriate (the tolerances assume the requested changes to Section B have been made):

Sugar Beet, Top	1.5 ppm
Sugar Beet, Root	0.9 ppm
Sugar Beet, Molasses	5.0 ppm
Canola Seed	0.4 ppm
Canola, Meal	1.1 ppm
*Potato	0.8 ppm
*Potato, chip	1.6 ppm
*Potato, granules/flakes	2.0 ppm

*Tolerance expression for the combined residues of glufosinate ammonium and 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents (non-transgenic crop).

A human-health risk assessment will be prepared as a separate document.

CONCLUSIONS

1a. The requested changes to the Rely® and Liberty™ labels have been made. The deficiencies identified in the original memo are resolved.

1b. The petitioner added information to the canola portion of the Liberty™ label allowing a higher application rate if the canola seed is retained for planting in the future. The Chemistry Science Advisory Committee discussed this issue and determined that canola grown for seed is a food use and therefore requires a tolerance (Chem SAC Minutes, 21-Jul-1999). The information pertaining to the higher use rate for canola grown for seed should be eliminated from the Liberty™ label. Additionally, the "Restrictions to the Directions for Use" section of the Liberty™ label for sugar beet and canola indicates application rates in ounces/acre. The units for application rates should be fluid ounces/acre. Finally, the restricted entry interval for workers should be increased from 12 to 24 hours on both the Rely® and Liberty™ labels (Occupational/Residential Exposure and Risk Assessment, D258415 and D258416, M. Christian, 6-Aug-1999). The petitioner should submit a revised Section B.

2. The deficiency related to a description of the confirmatory technique has been resolved. The Analytical Chemistry Branch (ACB) has not completed the validation procedures for methods BK/04/95 or HRAV-24. Given that the registrant has provided concurrent fortification data to demonstrate that BK/04/95 and HRAV-24 are adequate for data collection purposes and these methods are a modification of the current tolerance enforcement method, HED concludes that they are suitable enforcement methods to support tolerances associated with a conditional registration on potatoes, transgenic sugar beets and transgenic canola. As a condition of the registration, HED will require a successful petition method validation and the registrant will be required to make any necessary modifications to the method resulting from petition method validation.

3. A Section F, indicating the appropriate metabolites and tolerances for sugar beet, canola and potato commodities, has been submitted.

4. A storage stability study for Sugar Beet Processed Commodities (sugar, pulp and molasses; 3 months) is required. Pending submission and evaluation of this data, HED concludes that glufosinate ammonium and its metabolites do not concentrate in sugar beet pulp or sugar and the petitioners proposed sugar beet molasses tolerance of 5.0 ppm is appropriate.

DETAILED CONSIDERATIONS

Deficiency - Conclusions 2a, 2b and 2c (from D258075, T. Bloem, 28-Jul-1999)

2a The sugar beet portion of the Liberty™ Herbicide label should be amended to indicate in the "Special Notes" section that the maximum single application rate is 42 fluid ounces/acre (0.55 lbs ai/acre).

2b. The maximum seasonal application rate for canola is listed as 0.89 lbs ai/acre in the application timing section and 0.84 lbs ai/acre in the special notes section (0.89 lbs ai/acre will be assumed to be correct). The petitioner indicated that only the spring variety of canola has been genetically modified for tolerance to glufosinate ammonium. In Region 2, canola is only planted in the winter months (winter variety of canola) due to the unfavorable climate for canola in the summer. Therefore, the petitioner is not requesting registration of transgenic canola in Region 2. The canola portion of the Liberty™ Herbicide label should be amended to indicate in the "Special Notes" section that use of this product on transgenic canola in Region 2 is prohibited.

2c. Both the Rely® Herbicide and Liberty™ Herbicide labels should be amended to indicate a 120 day plant back interval for all crops except wheat where a 70 day plant back interval is appropriate.

Petitioner's Response: Submission of Revised Section B. The following information was added to the canola portion of the Liberty™ label, "Do not apply......more than 120 ounces per acre of Liberty Herbicide for segregate control during seed production per growing season". This increased rate (1.56 lbs/acre/season) is addressed a second time in an added section titled "Rate Recommendation for Use in Canola Seed Propagation" which states the following:

> For the detection and control of susceptible canola "segregates" during canola seed production only, Liberty Herbicide may be applied at up to 40 fluid ounces (2.5 pints) per acre on canola from the cotyledon stage to the early bolting stage of the canola. Applications may be repeated, if necessary, up to three times in one growing season.
>
> Do not apply more than 120 ounces of product per acre to canola being grown for seed production in one growing season.

HED's Conclusions: The requested changes to the Rely® and Liberty™ labels have been made. The deficiencies identified in the original memo are resolved.

The petitioner added information to the canola portion of the Liberty™ label allowing a higher application rate if the canola seed is retained for planting in the future. The Chemistry Science Advisory Committee (Chem SAC) recently discussed the food/non-food status of canola grown for seed. Chem SAC determined the following (Chem SAC Minutes, 21-Jul-1999):

> With a large acreage crop for which the seed is a significant food item and the sole reason the crop is grown in the first place, the SAC does not believe it is practical to prevent all the seed harvested from the treated crop from being diverted to food use. We are concerned with the precedent that would be set if these uses were classified as non-food uses. Nonfood uses may then be sought on even larger crops such as wheat and corn. Our guidelines state that there is little chance of calling applications to crops grown for seed nonfood uses when the seed is a major RAC (e.g., grains, beans, peas). It was specifically pointed out today by one chemist that a wheat hybridizing agent was registered a few years ago as a food use and tolerances established. We will continue to take the position that applications to such crops grown for seed are food uses requiring a tolerance (or exemption from tolerance if permitted by toxicological considerations).

The information pertaining to the higher application rate for canola grown for seed should be eliminated from the Liberty™ label. Additionally, the "Restrictions to the Directions for Use" section of the Liberty™ label for sugar beet and canola indicates application rates in ounces/acre. The units for application rates should be fluid ounces/acre. Finally, the restricted entry interval for workers should be increased from 12 to 24 hours on both the Rely® and Liberty™ labels (Occupational/Residential Exposure and Risk Assessment, D258415 and D258416, M. Christian, 6-Aug-1999). The petitioner should submit a revised Section B.

Deficiency - Conclusion 5d (from D257629, D257628, T. Bloem, 9-Jul-1999)

5d. Given that the registrant has provided concurrent fortification data to demonstrate that BK/04/95 and HRAV-24 are adequate for data collection purposes and these methods are a modification of the current tolerance enforcement method, HED concludes that they are suitable enforcement methods to support tolerances associated with a conditional registration on potatoes, transgenic sugar beets and transgenic canola. As a condition of the registration, HED will require a successful petition method validation and the registrant will be required to make any necessary modifications to the method resulting from petition method validation. Additionally, a complete description of the GC/MS confirmatory technique should be submitted by the petitioner.

Petitioner's Response: The petitioner provided the instrument model and GC conditions along with mass spectra for the parent and two metabolites. This information was taken from the metabolism study performed on transgenic field corn (MRID 43515602).

HED's Conclusions: The deficiency related to a description of the confirmatory technique has been resolved. ACB has not completed the validation procedure for BK/04/95 or HRAV-24. Therefore, the petitioner has not submitted a final version of these methods.

Deficiency - Conclusions 9f, 9i, 10c and 10i (from D257629, D257628, T. Bloem, 9-Jul-1999)

9f. HED concludes that based on the submitted field trial data, the appropriate tolerance in/on sugar beet tops and roots, as result of the application of glufosinate ammonium as defined in this petition, is 1.5 ppm and 0.9 ppm, respectively. The petitioner must submit a revised Section F proposing a 1.5 ppm tolerance in/on sugar beet tops and a 0.9 ppm tolerance in/on sugar beet roots for the combined residues of glufosinate ammonium and its metabolites 3-methylphosphinico propionic acid and N-acetyl glufosinate expressed as glufosinate free acid equivalents.

9i. HED concludes that based on the submitted field trial data, the appropriate tolerance in/on potatoes, as result of the application of glufosinate ammonium as defined in this petition, is 0.8 ppm. The petitioner must submit a revised Section F proposing a 0.8 ppm tolerance in/on potatoes for the combined residues of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents.

10c. HED concludes that the appropriate tolerance in/on canola meal, as a result of the application of glufosinate ammonium to canola as defined in this petition, is 1.1 ppm. The petitioner must submit a revised Section F proposing a canola meal tolerance of 1.1 ppm for the combined residues of glufosinate ammonium and its metabolites N-acetyl glufosinate ammonium and 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents.

10i. HED concludes that the appropriate tolerance in/on potato chips and potato granuales/flakes, as a result of the application of glufosinate ammonium to potatoes as defined in this petition, is 1.6 ppm and 2.0 ppm, respectively. The petitioner must submit a revised Section F proposing a potato chip tolerance of 1.6 ppm and a potato granule/flake tolerance of 2.0 ppm for the combined residues of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid expressed as glufosinate free acid equivalents.

Petitioner's Response: The petitioner submitted a revised Section F.

HED's Conclusions: The revised Section F indicates the appropriate metabolites and tolerances. These deficiencies have been resolved.

Deficiency - Conclusions 9f, 9i, 10c and 10i (from D257629, D257628, T. Bloem, 9-Jul-1999)

10f. HED will not be opposed to conditional registration of glufosinate ammonium on transgenic sugar beets. Unconditional registration may be granted upon validation of the three month storage interval for the processed commodities (sugar, pulp and molasses). Pending submission and evaluation of this data, HED concludes that the petitioners proposed sugar beet molasses tolerance of 5.0 ppm is appropriate.

Petitioner's Response: no response

HED's Conclusions: The requested information has not been provided. The deficiency remains outstanding.

cc: PP 7F04910 & 8F04997, T. Bloem (RAB1)
RDI: K. Whitby (19-Aug-1999), G. Kramer (19-Aug-1999), RAB1 Chemists (19-Aug-1999)
T. Bloem:806R:CM#2:(703)-605-0217

013720

Attachment 5: Acute and Chronic Dietary Exposure Analysis

D257266, T. Bloem, 19-July-1999

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

19-July-1999

MEMORANDUM

SUBJECT: PP# 7F04910 and 8F04997: **Glufosinate Ammonium Acute and Chronic Dietary Exposure Analysis.** Chemical 128850. DP Barcode D257266. Case 289177. Submission S529287.

FROM: Tom Bloem, Chemist
RAB1/HED (7509C)

THRU: Melba Morrow, D.V.M., Branch Senior Scientist, RAB1/HED (7509C)
Sheila Piper, Chemist, CEB1/HED (7509C)
William Cutchin, Chemist, RAB2/HED (7509C)

TO: Tom Bloem, Chemist
RAB1/HED (7509C)

Action Requested

AgrEvo USA Company has requested a Section 3 registration for use of glufosinate ammonium on potatoes, transgenic sugar beets and transgenic canola (PP#s 7F04910 & 8F04997) and the State of Minnesota has requested a Section 18 exemption for use of glufosinate ammonium on transgenic sweet corn. Acute and chronic dietary exposure analyses are requested.

Executive Summary

Both the acute and chronic DEEM™ analyses used consumption data from USDA's 1989-1992 nationwide Continuing Survey for Food Intake by Individuals (CSFII).

The acute dietary exposure analysis for females 13+ (no acute dietary endpoint was identified for the general US population including infants and children) assumed tolerance level residues and 100% crop treated for all registered and proposed commodities (Tier 1 analysis). The most highly exposed population was females 13+/nursing at 58% acute population adjusted dose (aPAD, 0.012131 mg/kg/day, 95th percentile). Acute dietary food exposure to glufosinate ammonium is below HEDs level of concern.

The chronic dietary exposure analysis assumed tolerance level residues for all registered and proposed commodities. The weighted average percent crop treated was incorporated for all registered commodities (Tier 2 analysis). The most highly exposed population was children 1-6 years old at 71% cPAD (0.004974 mg/kg/day). Chronic dietary food exposure to glufosinate ammonium is below HEDs level of concern.

Toxicological Information

The toxicological data base for glufosinate ammonium was evaluated by Hazard Identification Assessment Review Committee on May 5, 1999. The dietary endpoints chosen are outlined in the table below. The FQPA Safety Factor Committee met on May 10, 1999 to evaluate the hazard and exposure data for glufosinate ammonium and recommended that the FQPA Safety Factor be reduced to 3x in assessing the risk posed by this chemical (3x applicable to all populations subgroups and risk assessments).

<table>
<tr><th>exposure scenario</th><th>dose (mg/kg/day)</th><th>endpoint</th><th>study</th></tr>
<tr><td rowspan="2">acute dietary</td><td rowspan="2">NOAEL = 6.3
[1]UF = 300</td><td>LOAEL = 20 mg/kg/day based on decreased fetal body weight and increased fetal death</td><td>developmental toxicity–rabbit</td></tr>
<tr><td colspan="2">RfD = 0.063
acute population adjusted dose (aPAD) = 0.021 mg/kg (females 13+only)
no Acute RfD established for the general population including infants and children</td></tr>
<tr><td rowspan="2">chronic dietary (non-cancer)</td><td rowspan="2">NOAEL = 2.1
[1]UF = 300</td><td>LOAEL = 6.8 / 8.2 m mg/kg/day in males / females based on increased kidney weight and kidney/brain weight in males at 52 weeks, and decreased survival in females at 130 weeks.</td><td>Two-year chronic toxicity/oncogenicity in rat</td></tr>
<tr><td colspan="2">RfD = 0.021
chronic population adjusted dose (cPAD) = 0.007 mg/kg day</td></tr>
<tr><td>chronic dietary (cancer)</td><td colspan="3">glufosinate ammonium did not demonstrate evidence of carcinogenic potential</td></tr>
</table>

[1] 100x for intra and inter species variation; 3x FQPA Safety Factor

Residue Information

Time-limited tolerances are established for the combined residues of glufosinate ammonium and its metabolite, 3-methylphosphinico propionic acid, in/on apples (0.05 ppm), grapes (0.05 ppm), bananas (0.2 ppm) and the tree nut group (0.1 ppm). Time limited tolerances are also established for these two compounds as a result of secondary residues in milk (0.02 ppm), eggs (0.05 ppm), and the meat (0.05 ppm), fat (0.05 ppm) and meat byproducts (0.10 ppm) of ruminants and poultry (40 CFR 180.473(a) and (b)). Glufosinate ammonium is registered for use on transgenic soybeans and corn. The tolerance expression for commodities derived from transgenic crops includes glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate. Time limited tolerances are established in/on transgenic field corn grain (0.2 ppm) and transgenic soybeans (2.0 ppm) (40 CFR 180.473(c)). A Section 18 request from Wisconsin for use of glufosinate ammonium on transgenic sweet corn has been approved (D253382; 4.0 ppm tolerance).

The tolerance established on sweet corn (4.0 ppm) as a result of the Wisconsin Section 18 is applicable to the Minnesota Section 18 sweet corn request (same application scenarios). Based on the submitted crop field trial and processing studies, the following tolerances for the combined residues of glufosinate ammonium, 3-methylphosphinico propionic acid and N-acetyl glufosinate, are appropriate:

Sugar Beet, Root .... 0.9 ppm
Sugar Beet, Molasses .... 5.0 ppm
Canola Seed .... 0.4 ppm
*Potato .... 0.8 ppm
*Potato, processed .... 1.6 ppm
*Potato, flakes .... 2.0 ppm

** tolerance for combined residues of glufosinate ammonium and its metabolite 3-methylphosphinico propionic acid (non-transgenic crop)*

The acute dietary exposure analysis assumed tolerance level residues and 100% crop treatment for all registered and proposed commodities (Tier 1 analysis).

The chronic dietary exposure analysis assumed tolerance level residues for all registered and proposed commodities and incorporated the weighted average percent crop treated (BEAD, A. Halvorson, 15-Apr-1999; Attachment #3) for all registered commodities (Tier 2 analysis). Sweet corn percent crop treated was maintained at 100% due to the possibility that other states may request the same Section 18.

Acute and Chronic Dietary Exposure

Summary of Results from Acute DEEM™ Analysis for Glufosinate Ammonium

subgroups	exposure[1] (mg/kg/day)	% aPAD
Females (13+, preg., not nursing)	0.008179	39
Females (13+, nursing)	0.012131	58
Females (13-19 yrs., not preg., not nursing)	0.008425	40
Females (20+ years, not preg., not nursing)	0.007086	34
Females (13-50 years)	0.007751	37

[1] 95th percentile exposures, consumption data from USDA's 1989-1992 nationwide Continuing Survey for Food Intake by Individuals (CSFII)

Summary of Results from Chronic DEEM™ Analysis for Glufosinate ammonium

[1]subgroups	exposure[2] (mg/kg/day)	% cPAD
U.S. Population (48 states)	0.002120	30
Non-Hispanic blacks	0.002246	32
Non-Hispanic/non-white/non-black	0.002256	32
Non-Hispanic whites	0.002132	31
Children (1-6 years)	0.004974	71
Females (13+ nursing)	0.002035	29
Males 13-19 yrs	0.002449	35

[1] The subgroups listed above are the following: (1) US Population, (2) the other general subgroups for which the %cPAD is greater than that of the US Population and (3) the most highly exposed population among infants and children, females, and males.

[2] consumption data from USDA's 1989-1992 nationwide Continuing Survey for Food Intake by Individuals (CSFII)

Results and Discussion

Both the acute and chronic DEEM^{TM} analyses used consumption data from USDA's 1989-1992 nationwide Continuing Survey for Food Intake by Individuals (CSFII).

The acute dietary exposure analysis for females 13+ (no acute dietary endpoint was identified for the general US population including infants and children) assumed tolerance level residues and 100% crop treated for all registered and proposed commodities (Tier 1 analysis). The most highly exposed population was females 13+/nursing at 58% acute population adjusted dose (aPAD, 0.012131 mg/kg/day, 95th percentile). Acute dietary food exposure to glufosinate ammonium is below HEDs level of concem.

The chronic dietary exposure analysis assumed tolerance level residues for all registered and proposed commodities. The weighted average percent crop treated was incorporated for all registered commodities (Tier 2 analysis). The most highly exposed population was children 1-6 years old at 71% cPAD (0.004974 mg/kg/day). Chronic dietary food exposure to glufosinate ammonium is below HEDs level of concern.

Attachment 1:	Acute Dietary Exposure Estimates and Residue File
Attachment 2:	Chronic Dietary Exposure Estimates and Residue File
Attachment 3:	% crop treated; BEAD, A. Halvorson, 15-Apr-1999

cc with attachments: M. Sahafeyen (CEB1)
RDI: S. Piper & W. Cutchin (28-Jun-1999), M. Morrow (29-Jun-1999)
T. Bloem:CM#2: 806-R:(703)605-0217

Attachment 1: Acute Dietary Exposure Estimates and Residue File

U.S. Environmental Protection Agency Ver. 6.78
DEEM ACUTE analysis for GLUFOSINATE AMMONIUM (1989-92 data)
Residue file: 128850a.r96 Adjustment factor #2 NOT used.
Analysis Date: 07-14-1999/08:59:57 Residue file dated: 07-14-1999/08:54:56/8
Acute Reference Dose (aRfD) = 0.021000 mg/kg body-wt/day
NOEL (Acute) = 6.300000 mg/kg body-wt/day
Run Comment: acute & chronic UF; 10(intra) 10(inter) 3(FQPA); total UF 300

Summary calculations:

95th Percentile			99th Percentile			99.9th Percentile		
Exposure	% aRfD	MOE	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE
Females (13+/preg/not nsg):								
0.008179	38.95	770	0.012634	60.16	498	0.013158	62.66	478
Females (13+/nursing):								
0.012131	57.77	519	0.013682	65.15	460	0.017500	83.33	360
Females (13-19 yrs/np/nn):								
0.008425	40.12	747	0.018479	87.99	340	0.026188	124.70	240
Females (20+ years/np/nn):								
0.007086	33.74	889	0.013461	64.10	468	0.024239	115.42	259
Females (13-50 years):								
0.007751	36.91	812	0.014686	69.93	428	0.025741	122.58	244

Filename: C:\DEEM\resdata\128850a.r96
Chemical name: glufosinate ammonium
RfD(Chronic): .007 mg/kg bw/day NOEL(Chronic): 2.1 mg/kg bw/day
RfD(Acute): .021 mg/kg bw/day NOEL(Acute): 6.3 mg/kg bw/day
Date created/last modified: 07-14-1999/08:54:56/8 Program ver. 6.77
Comment: acute & chronic UF; 10(intra) 10(inter) 3(FQPA); total UF 300

Food Code	Crop Grp	Food Name	RESIDUE (ppm)	RDF #	Adj.Factors #1	#2	Comment
40	14	Almonds	0.100000	0	1.000	1.000	
52	11	Apples	0.050000	0	1.000	1.000	
53	11	Apples-dried	0.050000	0	8.000	1.000	
54	11	Apples-juice/cider	0.050000	0	1.300	1.000	
377	11	Apples-juice-concentrate	0.050000	0	3.900	1.000	
72	O	Bananas	0.200000	0	1.000	1.000	
		Full comment: residue expected in pulp after peel is removed					
73	O	Bananas-dried	0.200000	0	3.900	1.000	
		Full comment: residue expected in pulp after peel is removed					
378	O	Bananas-juice	0.200000	0	1.000	1.000	
		Full comment: residue expected in pulp after peel is removed					
51	14	Beech-nuts	0.100000	0	1.000	1.000	
323	M	Beef-dried	0.050000	0	1.920	1.000	
324	M	Beef-fat w/o bones	0.050000	0	1.000	1.000	
325	M	Beef-kidney	0.100000	0	1.000	1.000	
327	M	Beef-lean (fat/free) w/o bones	0.050000	0	1.000	1.000	
326	M	Beef-liver	0.100000	0	1.000	1.000	
321	M	Beef-meat byproducts	0.100000	0	1.000	1.000	
322	M	Beef-other organ meats	0.100000	0	1.000	1.000	
41	14	Brazil nuts	0.100000	0	1.000	1.000	
49	14	Butter nuts	0.100000	0	1.000	1.000	
301	O	Canola oil (rape seed oil)	0.400000	0	1.000	1.000	7F04910, 8F04997
42	14	Cashews	0.100000	0	1.000	1.000	
43	14	Chestnuts	0.100000	0	1.000	1.000	
366	P	Chicken-byproducts	0.100000	0	1.000	1.000	
368	P	Chicken-fat w/o bones	0.050000	0	1.000	1.000	
367	P	Chicken-giblets(liver)	0.100000	0	1.000	1.000	
385	P	Chicken-giblets (excl. liver)	0.100000	0	1.000	1.000	
369	P	Chicken-lean/fat free w/o bones	0.050000	0	1.000	1.000	
267	15	Corn grain-bran	0.200000	0	1.000	1.000	
266	15	Corn grain-endosperm	0.200000	0	1.000	1.000	
289	15	Corn grain-oil	0.200000	0	1.000	1.000	
268	15	Corn grain/sugar/hfcs	0.200000	0	1.500	1.000	
388	15	Corn grain/sugar-molasses	0.200000	0	1.500	1.000	
238	15	Corn/sweet					
		11-Uncooked	4.000000	0	1.000	1.000	
		12-Cooked: NFS	4.000000	0	1.000	1.000	
		13-Baked	4.000000	0	1.000	1.000	
		14-Boiled	4.000000	0	1.000	1.000	
		32-Canned: Cooked	4.000000	0	1.000	1.000	
		34-Canned: Boiled	4.000000	0	1.000	1.000	
		35-Canned: Fried	4.000000	0	1.000	1.000	
		42-Frozen: Cooked	4.000000	0	1.000	1.000	
364	P	Eggs-white only	0.050000	0	1.000	1.000	
363	P	Eggs-whole	0.050000	0	1.000	1.000	
365	P	Eggs-yolk only	0.050000	0	1.000	1.000	
44	14	Filberts (hazelnuts)	0.100000	0	1.000	1.000	
330	M	Goat-fat w/o bone	0.050000	0	1.000	1.000	
331	M	Goat-kidney	0.100000	0	1.000	1.000	
333	M	Goat-lean (fat/free) w/o bone	0.050000	0	1.000	1.000	
332	M	Goat-liver	0.100000	0	1.000	1.000	
328	M	Goat-meat byproducts	0.100000	0	1.000	1.000	
329	M	Goat-other organ meats	0.100000	0	1.000	1.000	
13	O	Grapes	0.050000	0	1.000	1.000	
15	O	Grapes-juice	0.050000	0	1.200	1.000	
392	O	Grapes-juice-concentrate	0.050000	0	3.600	1.000	
195	O	Grapes-leaves	0.050000	0	1.000	1.000	
14	O	Grapes-raisins	0.050000	0	4.300	1.000	
315	O	Grapes-wine and sherry	0.050000	0	1.000	1.000	
45	14	Hickory nuts	0.100000	0	1.000	1.000	
334	M	Horsemeat	0.050000	0	1.000	1.000	
46	14	Macadamia nuts (bush nuts)	0.100000	0	1.000	1.000	

398	D	Milk-based water	0.020000	0	1.000	1.000	
319	D	Milk-fat solids	0.020000	0	1.000	1.000	
318	D	Milk-nonfat solids	0.020000	0	1.000	1.000	
320	D	Milk sugar (lactose)	0.020000	0	1.000	1.000	
47	14	Pecans	0.100000	0	1.000	1.000	
344	M	Pork-fat w/o bone	0.050000	0	1.000	1.000	
345	M	Pork-kidney	0.100000	0	1.000	1.000	
347	M	Pork-lean (fat free) w/o bone	0.050000	0	1.000	1.000	
346	M	Pork-liver	0.100000	0	1.000	1.000	
342	M	Pork-meat byproducts	0.100000	0	1.000	1.000	
343	M	Pork-other organ meats	0.100000	0	1.000	1.000	
210	1C	Potatoes/white-dry	2.000000	0	1.000	1.000	7F04910, 8F04997
209	1C	Potatoes/white-peeled	0.800000	0	1.000	1.000	7F04910, 8F04997
211	1C	Potatoes/white-peel only	0.800000	0	1.000	1.000	7F04910, 8F04997
208	1C	Potatoes/white-unspecified	2.000000	0	1.000	1.000	7F04910, 8F04997
207	1C	Potatoes/white-whole	0.800000	0	1.000	1.000	7F04910, 8F04997
362	P	Poultry-other-fat w/o bones	0.050000	0	1.000	1.000	
361	P	Poultry-other-giblets(liver)	0.100000	0	1.000	1.000	
360	P	Poultry-other-lean (fat free) w/	0.050000	0	1.000	1.000	
338	M	Sheep-fat w/o bone	0.050000	0	1.000	1.000	
339	M	Sheep-kidney	0.100000	0	1.000	1.000	
341	M	Sheep-lean (fat free) w/o bone	0.050000	0	1.000	1.000	
340	M	Sheep-liver	0.100000	0	1.000	1.000	
336	M	Sheep-meat byproducts	0.100000	0	1.000	1.000	
337	M	Sheep-other organ meats	0.100000	0	1.000	1.000	
303	6A	Soybean-other	2.000000	0	1.000	1.000	
307	6A	Soybeans-flour (defatted)	2.000000	0	1.000	1.000	
306	6A	Soybeans-flour (low fat)	2.000000	0	1.000	1.000	
305	6A	Soybeans-flour (full fat)	2.000000	0	1.000	1.000	
304	6A	Soybeans-mature seeds dry	2.000000	0	1.000	1.000	
297	6A	Soybeans-oil	2.000000	0	1.000	1.000	
482	O	Soybeans-protein isolate	2.000000	0	1.000	1.000	
255	6A	Soybeans-sprouted seeds	2.000000	0	0.330	1.000	
282	1A	Sugar-beet	0.900000	0	1.000	1.000	7F04910, 8F04997
379	1A	Sugar-beet-molasses	5.000000	0	1.000	1.000	7F04910, 8F04997
355	P	Turkey-byproducts	0.100000	0	1.000	1.000	
357	P	Turkey--fat w/o bones	0.050000	0	1.000	1.000	
356	P	Turkey-giblets (liver)	0.100000	0	1.000	1.000	
358	P	Turkey- lean/fat free w/o bones	0.050000	0	1.000	1.000	
449	P	Turkey-other organ meats	0.100000	0	1.000	1.000	
429	M	Veal-dried	0.050000	0	1.920	1.000	
424	M	Veal-fat w/o bones	0.050000	0	1.000	1.000	
426	M	Veal-kidney	0.100000	0	1.000	1.000	
425	M	Veal-lean (fat free) w/o bones	0.050000	0	1.000	1.000	
427	M	Veal-liver	0.100000	0	1.000	1.000	
430	M	Veal-meat byproducts	0.100000	0	1.000	1.000	
428	M	Veal-other organ meats	0.100000	0	1.000	1.000	
431	14	Walnut oil	0.100000	0	1.000	1.000	
48	14	Walnuts	0.100000	0	1.000	1.000	

Attachment 2: **Chronic Dietary Exposure Estimates and Residue File**

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U.S. Environmental Protection Agency                          Ver. 6.76
DEEM Chronic analysis for GLUFOSINATE AMMONIUM             (1989-92 data)
Residue file name: C:\DEEM\resdata\128850c.r96      Adjustment factor #2 used.
Analysis Date 07-14-1999/08:58:01     Residue file dated: 07-14-1999/08:53:45/8
Reference dose (RfD, CHRONIC) = .007 mg/kg bw/day
COMMENT 1: acute & chronic UF; 10(intra-) 10(inter) 3(FQPA); total UF 300
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                     Total exposure by population subgroup
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Population Subgroup	Total Exposure mg/kg body wt/day	Percent of Rfd
U.S. Population (total)	0.002120	30.3%
U.S. Population (spring season)	0.002059	29.4%
U.S. Population (summer season)	0.002189	31.3%
U.S. Population (autumn season)	0.002062	29.5%
U.S. Population (winter season)	0.002162	30.9%
Northeast region	0.002107	30.1%
Midwest region	0.002388	34.1%
Southern region	0.002123	30.3%
Western region	0.001807	25.8%
Hispanics	0.001786	25.5%
Non-hispanic whites	0.002132	30.5%
Non-hispanic blacks	0.002246	32.1%
Non-hisp/non-white/non-black)	0.002256	32.2%
All infants (< 1 year)	0.001930	27.6%
Nursing infants	0.000599	8.6%
Non-nursing infants	0.002491	35.6%
Children 1-6 yrs	0.004974	71.1%
Children 7-12 yrs	0.003480	49.7%
Females 13-19(not preg or nursing)	0.001800	25.7%
Females 20+ (not preg or nursing)	0.001476	21.1%
Females 13-50 yrs	0.001570	22.4%
Females 13+ (preg/not nursing)	0.001624	23.2%
Females 13+ (nursing)	0.002035	29.1%
Males 13-19 yrs	0.002449	35.0%
Males 20+ yrs	0.001645	23.5%
Seniors 55+	0.001553	22.2%
Pacific Region	0.001746	24.9%

Filename: C:\DEEM\resdata\128850c.r96
Chemical name: glufosinate ammonium
RfD(Chronic): .007 mg/kg bw/day NOEL(Chronic): 2.1 mg/kg bw/day
RfD(Acute): .021 mg/kg bw/day NOEL(Acute): 6.3 mg/kg bw/day
Date created/last modified: 07-14-1999/08:53:45/8 Program ver. 6.77
Comment: acute & chronic UF; 10(intra-) 10(inter) 3(FQPA); total UF 300

Food Code	Crop Grp	Food Name	RESIDUE (ppm)	RDF #	Adj.Factors #1	#2	Comment
40	14	Almonds	0.100000	0	1.000	0.010	
52	11	Apples	0.050000	0	1.000	0.010	
53	11	Apples-dried	0.050000	0	8.000	0.010	
54	11	Apples-juice/cider	0.050000	0	1.300	0.010	
377	11	Apples-juice-concentrate	0.050000	0	3.900	0.010	
72	O	Bananas	0.200000	0	1.000	1.000	
		Full comment: residue expected in pulp after peel is removed					
73	O	Bananas-dried	0.200000	0	3.900	1.000	
		Full comment: residue expected in pulp after peel is removed					
378	O	Bananas-juice	0.200000	0	1.000	1.000	
		Full comment: residue expected in pulp after peel is removed					
51	14	Beech-nuts	0.100000	0	1.000	0.010	
323	M	Beef-dried	0.050000	0	1.920	1.000	
324	M	Beef-fat w/o bones	0.050000	0	1.000	1.000	
325	M	Beef-kidney	0.100000	0	1.000	1.000	
327	M	Beef-lean (fat/free) w/o bones	0.050000	0	1.000	1.000	
326	M	Beef-liver	0.100000	0	1.000	1.000	
321	M	Beef-meat byproducts	0.100000	0	1.000	1.000	
322	M	Beef-other organ meats	0.100000	0	1.000	1.000	
41	14	Brazil nuts	0.100000	0	1.000	0.010	
49	14	Butter nuts	0.100000	0	1.000	0.010	
301	O	Canola oil (rape seed oil)	0.400000	0	1.000	1.000	7F04910, 8F04997
42	14	Cashews	0.100000	0	1.000	0.010	
43	14	Chestnuts	0.100000	0	1.000	0.010	
366	P	Chicken-byproducts	0.100000	0	1.000	1.000	
368	P	Chicken-fat w/o bones	0.050000	0	1.000	1.000	
367	P	Chicken-giblets(liver)	0.100000	0	1.000	1.000	
385	P	Chicken-giblets (excl. liver)	0.100000	0	1.000	1.000	
369	P	Chicken-lean/fat free w/o bones	0.050000	0	1.000	1.000	
267	15	Corn grain-bran	0.200000	0	1.000	0.026	
266	15	Corn grain-endosperm	0.200000	0	1.000	0.026	
289	15	Corn grain-oil	0.200000	0	1.000	0.026	
268	15	Corn grain/sugar/hfcs	0.200000	0	1.500	0.026	
388	15	Corn grain/sugar-molasses	0.200000	0	1.500	0.026	
238	15	Corn/sweet					
		11-Uncooked	4.000000	0	1.000	1.000	
		12-Cooked: NFS	4.000000	0	1.000	1.000	
		13-Baked	4.000000	0	1.000	1.000	
		14-Boiled	4.000000	0	1.000	1.000	
		32-Canned: Cooked	4.000000	0	1.000	1.000	
		34-Canned: Boiled	4.000000	0	1.000	1.000	
		35-Canned: Fried	4.000000	0	1.000	1.000	
		42-Frozen: Cooked	4.000000	0	1.000	1.000	
364	P	Eggs-white only	0.050000	0	1.000	1.000	
363	P	Eggs-whole	0.050000	0	1.000	1.000	
365	P	Eggs-yolk only	0.050000	0	1.000	1.000	
44	14	Filberts (hazelnuts)	0.100000	0	1.000	0.010	
330	M	Goat-fat w/o bone	0.050000	0	1.000	1.000	
331	M	Goat-kidney	0.100000	0	1.000	1.000	
333	M	Goat-lean (fat/free) w/o bone	0.050000	0	1.000	1.000	
332	M	Goat-liver	0.100000	0	1.000	1.000	
328	M	Goat-meat byproducts	0.100000	0	1.000	1.000	
329	M	Goat-other organ meats	0.100000	0	1.000	1.000	
13	O	Grapes	0.050000	0	1.000	0.010	
15	O	Grapes-juice	0.050000	0	1.200	0.010	
392	O	Grapes-juice-concentrate	0.050000	0	3.600	0.010	
195	O	Grapes-leaves	0.050000	0	1.000	0.010	
14	O	Grapes-raisins	0.050000	0	4.300	0.010	
315	O	Grapes-wine and sherry	0.050000	0	1.000	0.010	
45	14	Hickory nuts	0.100000	0	1.000	0.010	
334	M	Horsemeat	0.050000	0	1.000	1.000	
46	14	Macadamia nuts (bush nuts)	0.100000	0	1.000	0.010	

398	D	Milk-based water	0.020000	0	1.000	1.000	
319	D	Milk-fat solids	0.020000	0	1.000	1.000	
318	D	Milk-nonfat solids	0.020000	0	1.000	1.000	
320	D	Milk sugar (lactose)	0.020000	0	1.000	1.000	
47	14	Pecans	0.100000	0	1.000	0.010	
344	M	Pork-fat w/o bone	0.050000	0	1.000	1.000	
345	M	Pork-kidney	0.100000	0	1.000	1.000	
347	M	Pork-lean (fat free) w/o bone	0.050000	0	1.000	1.000	
346	M	Pork-liver	0.100000	0	1.000	1.000	
342	M	Pork-meat byproducts	0.100000	0	1.000	1.000	
343	M	Pork-other organ meats	0.100000	0	1.000	1.000	
210	1C	Potatoes/white-dry	2.000000	0	1.000	1.000	7F04910, 8F04997
209	1C	~~Potatoes/white-peeled~~	~~0.800000~~	~~0~~	1.000	~~1.000~~	~~7F04910~~, 8F04997
211	1C	Potatoes/white-peel only	0.800000	0	1.000	1.000	7F04910, 8F04997
208	1C	Potatoes/white-unspecified	2.000000	0	1.000	1.000	7F04910, 8F04997
207	1C	Potatoes/white-whole	0.800000	0	1.000	1.000	7F04910, 8F04997
362	P	Poultry-other-fat w/o bones	0.050000	0	1.000	1.000	
361	P	Poultry-other-giblets(liver)	0.100000	0	1.000	1.000	
360	P	Poultry-other-lean (fat free) w/	0.050000	0	1.000	1.000	
338	M	Sheep-fat w/o bone	0.050000	0	1.000	1.000	
339	M	Sheep-kidney	0.100000	0	1.000	1.000	
341	M	Sheep-lean (fat free) w/o bone	0.050000	0	1.000	1.000	
340	M	Sheep-liver	0.100000	0	1.000	1.000	
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337	M	Sheep-other organ meats	0.100000	0	1.000	1.000	
303	6A	Soybean-other	2.000000	0	1.000	0.010	
307	6A	Soybeans-flour (defatted)	2.000000	0	1.000	0.010	
306	6A	Soybeans-flour (low fat)	2.000000	0	1.000	0.010	
305	6A	Soybeans-flour (full fat)	2.000000	0	1.000	0.010	
304	6A	Soybeans-mature seeds dry	2.000000	0	1.000	0.010	
297	6A	Soybeans-oil	2.000000	0	1.000	0.010	
482	O	Soybeans-protein isolate	2.000000	0	1.000	0.010	
255	6A	Soybeans-sprouted seeds	2.000000	0	0.330	0.010	
282	1A	Sugar-beet	0.900000	0	1.000	1.000	7F04910, 8F04997
379	1A	Sugar-beet-molasses	5.000000	0	1.000	1.000	7F04910, 8F04997
355	P	Turkey-byproducts	0.100000	0	1.000	1.000	
357	P	Turkey--fat w/o bones	0.050000	0	1.000	1.000	
356	P	Turkey-giblets (liver)	0.100000	0	1.000	1.000	
358	P	Turkey- lean/fat free w/o bones	0.050000	0	1.000	1.000	
449	P	Turkey-other organ meats	0.100000	0	1.000	1.000	
429	M	Veal-dried	0.050000	0	1.920	1.000	
424	M	Veal-fat w/o bones	0.050000	0	1.000	1.000	
426	M	Veal-kidney	0.100000	0	1.000	1.000	
425	M	Veal-lean (fat free) w/o bones	0.050000	0	1.000	1.000	
427	M	Veal-liver	0.100000	0	1.000	1.000	
430	M	Veal-meat byproducts	0.100000	0	1.000	1.000	
428	M	Veal-other organ meats	0.100000	0	1.000	1.000	
431	14	Walnut oil	0.100000	0	1.000	0.010	
48	14	Walnuts	0.100000	0	1.000	0.010	

Attachment 3: **% crop treated; BEAD, A. Halvorson, 15-Apr-1999** 013728

GLUFOSINATE %CROP TREATED BASED ON 1995-1998 DATA, AGRICULTURAL CROPS
Alan Halvorson, EAB/BEAD, 4/15/99

		-- Wtd Average --		--- Maximum ---	
	A plntd (000)	A trtd (000)	% trtd (%)	A trtd (000)	% trtd (%)
ALMONDS	438	0	0.0%	0	0.0%
APPLES	635	2	0.3%	4	0.6%
CHERRIES	126	0	0.0%	0	0.0%
CORN	77,831	2,000	2.6%	3,100	4.0%
GRAPEVINES	876	0	0.0%	0	0.0%
LOTS/FARMSTEAD/ETC	22,848	0	0.0%	0	0.0%
PEACHES	235	0	0.0%	0	0.0%
PEARS	83	0	0.0%	0	0.0%
PECAN	494	0	0.0%	0	0.0%
PLUMS/PRUNES	139	0	0.0%	0	0.0%
SOYBEANS	67,593	10	0.01%	13	0.02%
WALNUTS	205	0	0.0%	0	0.0%
OTHER NUT TREES	114	0	0.0%	0	0.0%

Note -- Data indicate usage on corn has been increasing over the past few years

013729

Attachment 6: Tier II Estimated Environmental Concentrations

D250756 & D257381, L. Libelo (EFED)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

PC Code: 128850
DP Bar Code: D250756

MEMORANDUM

SUBJECT: Tier II Estimated Environmental Concentrations for Glufosinate-ammonium.

FROM: E. Laurence Libelo, Ph.D., Environmental Engineer
Environmental Risk Branch IV
Environmental Fate and Effects Division (7507C)

THROUGH: Mah T. Shamim, Ph.D., Chief
Environmental Risk Branch IV
Environmental Fate and Effects Division (7507C)

TO: Joanne Miller, Product Manager
Eugene Wilson
Herbicide Branch, Registration Division (7505C)

Clark Swentzel, Acting Chief
Olga Odiott
Registration Branch I
Health Effects Division (7509C)

This memo summarizes tier 1 ground water and tier 2 surface water estimated drinking water concentration values for use in FQPA assessments. The tier 1 ground water estimate was developed using the SCI-GROW program and was provided previously. The tier 2 surface water estimate was calculated using the PRZM/EXAMS model linkage. There are no refined tier 2 methods for ground water at this time. The SCI-GROW ground water concentration represents typical concentrations which may be expected to result from application of this chemical on as described in the RELY® label on apples, grapes and tree nuts. The tier 2 PRZM/EXAMS simulation represents application on apples in New York State and sugar beets in Minnesota. These values represent estimates of the concentration that might be found in surface or ground water as a result of use at the maximum label rates. The surface and ground water concentrations values are listed below and in Table 1. The surface water concentration value that should be used for acute human health risk assessment is the peak value of **34.1 µg/L** for parent glufosinate ammonium. The surface water value that should be used for chronic and cancer human health risk assessments is the long term average values of **0.79 µg/L.**

The SCI-GROW groundwater concentration value is **1.16 µg/L.** The chemical properties of this chemical lie outside the range of environmental fate data used to develop SCI-GROW and so requires extrapolation. This concentration value is therefore highly uncertain, and should be used with caution.

Table 1. Estimated environmental concentrations (drinking water) for glufosinate ammonium on apples in New York State and sugar beets in Minnesota.

Crop	1 in 10 Year Maximum Surface Concentration	Average of 36 Years of Daily Surface Concentration Values
Apples	34.1 µg/L	0.79 µg/L
Sugar Beets	7.1 µg/L	0.26 µg/L
SCI-GROW Groundwater Concentration	1.16 µg/L	

Tier 2 Surface Water Site/Scenario for Use of Glufosinate ammonium on Apples and Sugar Beets

One site/scenario was used to represent use of glufosinate ammonium on apples. It represents a 10 hectare field draining into a 1 hectare pond, 2 meters deep with no outlet. Inflow to the pond from runoff are assumed to be exactly balanced by losses due to evaporation and seepage. On the site it is assumed that grass covers the surface below the apples and that applied pesticide lands either the grass below.

The site is an orchard/vineyard in Columbia County, New York in MLRA 144B. The soil at the site is a Cabot silt loam. Data for this soil was taken from the PIC database and the 1987 National Resources Inventory. Cabot silt loam is hydrologic group D soil and SCS curve numbers were generated based on this grouping and the plant cover. A total of 3070 acres of apples, about 0.5% of the U.S. total, were grown in Columbia County in 1997 (USDA, NASS, Ag. Census). Weather data was taken from weather station W04725 in Albany, NY. The weather data file is part of the PRZM program and is used to represent the weather for MLRA R-144B. This site receives an annual average precipitation of about 93 cm of which 19% on the average leaves site as runoff. The chemical specific parameters used in PRZM3 and EXAMS to describe the scenario are tabulated in Table 2 attached. The site was selected to represent orchards and vineyards in the eastern United States that are likely to present high exposure to aquatic organisms.

A similar site/scenario was used to represent use on sugar beets in Minnesota. The site is in Polk Co., MN in MLRA F-56. The soil at the site is a Bearden silty clay loam. Data for this soil was taken from the PIC database and the 1987 National Resources Inventory. Bearden silty clay loam is a hydrologic group C soil and SCS curve numbers were generated based on this grouping and the plant cover. Polk Co. was selected as representative of major sugar beet growing areas. In 1997 106,430 acres of sugar beets, about 7% of total U.S. acreage were planted in the county (USDA, NASS Ag. Census). Weather data was taken from weather station W14914 in Fargo, ND. The weather data file is part of the PRZM program, and is used to represent the weather for MLRA F-56. The chemical specific parameters used in PRZM3 and EXAMS to describe the scenario are tabulated in Table 2.

Procedure

The PRZM simulation was run using 36 years of weather data encompassing the years from 1948 to 1983. The modeling assumed application of the pesticide three times per year both for apples and for sugar beets at the maximum allowable rate permitted by the label. These scenario assumes 5% spray drift directly to the pond with the remainder of the chemical reaching the water through runoff from rainfall events. The maximum concentration values in Table 1 above are the one-in-ten year return period values taken the REPORT.XMS file produced by EXAMS. These 10 year return concentrations (or 10% yearly exceedence EEC's) were calculated by linear interpolation between the third and fourth largest values.

Environmental Fate Input Values

Environmental fate inputs to the PRZM and EXAMS programs are listed along with their sources in Tables 2. Soil, cropping and management inputs to PRZM are those selected by the PIC (PRZM Input Collator) data base. EXAMS environment inputs are taken from the Georgia pond scenario.

Background Information on SCI-GROW:

SCI-GROW provides a groundwater screening exposure value to be used in determining the potential risk to human health from drinking water contaminated with the pesticide. The model generally under predicts the maximum concentration and actual concentrations can generally be expected to be higher. The calculated concentration is probably representative of concentrations that can be expected when the chemical is used in vulnerable areas.

Table 2. PRZM/EXAMS environmental fate input parameters for glufosinate ammonium

Parameter	Value	Data source
Molecular Weight	198.2	---
Solubility	1.63 kg/L	personal communication with Dr. Ian Kelly, AGREVO 5/19/99
Vapor Pressure (torr)	> 1x 10^{-6}	personal communication with AGREVO 5/19/99
Henry's Law Constant	1.19 x 10^{15}	Dr. Ian Kelly, AGREVO, FAX dated 5/19/99
pH 5 Hydrolysis Half-life (days)	stable	MRID 40345656, DER 9/22/88
pH 7 Hydrolysis Half-life (days)	stable	MRID 40345656, DER 9/22/88
pH 9 Hydrolysis Half-life (days)	stable	MRID 40345656, DER 9/22/88
Soil Photolysis Half-life (days)	stable	MRID 40345658
Aquatic Photolysis Half-life (days)	stable	MRID 40345657, DER 9/22/88
Aerobic Soil Metabolism (days)	23	MRID 40345659-A, DER 9/22/88
Aerobic Aquatic Metabolism Half-life	35	MRID 4034566, DER 9/22/88
Anaerobic Soil Metabolism Half-life	56	MRID 40501014, DER 9/22/88
Soil-Water Partitioning Coefficient (K_d)	0.98	MRID 40345662, DER 9/22/88

Table 3. Input Parameters for SCI-GROW (apples, grapes, and pecans).

Parameter	Value	Source
Chemical	Glufosinate ammonium	
Organic Carbon Partition Coefficient (K_{oc})	9.6 ml/g	MRID 40345662, DER 9/22/88
Aerobic Soil Metabolism Half-Life	14 days	MRID 40345659-A, DER 9/22/88
Application Rate	1.5 lb a.i./acre	RELY® Label
Maximum Application Per Year	4.5 lb/acre/year	RELY® Label

Scigrow Output

```
RUN No.   1 FOR Glufosinate ammoniumINPUT VALUES
--------------------------------------------------------------------
 APPL (#/AC)  APPL.  URATE    SOIL    SOIL  AEROBIC
 RATE           NO. (#/AC/YR)  KOC   METABOLISM (DAYS)
--------------------------------------------------------------------
   1.500       3       4.500        9.6       14.0

GROUND-WATER SCREENING CONCENTRATIONS IN PPB
--------------------------------------------------------
                 1.155603
--------------------------------------------------------
A=      9.000  B=     14.600  C=       .954  D=      1.164  RILP=      2.706
F=      -.590  G=       .257  URATE=      4.500  GWSC=        1.155603
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Attachment 7: Occupational/Residential Exposure and Risk Assessment

D258415 & D258416, M. Christian, 7-Sep-1999

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: September 7, 1999

Subject: Glufosinate Ammonium on Potatoes, Transgenic Sugar Beets and Transgenic Canola. **Occupational Exposure and Risk Assessment.** DP Barcode: D258415 and D258416. Chemical #: 128850. EPA Registration Numbers: 45639-187 (Rely®) and 45639-199 (Liberty™).

From: Myrta Christian, Biologist
Registration Action Branch I
Health Effects Division (7509C)

Through: Olga Odiott, Biologist
Registration Action Branch I
Health Effects Division (7509C)

Melba Morrow, Branch Senior Scientist
Registration Action Branch I
Health Effects Division (7509C)

To: Thomas Bloem, Chemist
Registration Action Branch I
Health Effects Division (7509C)

Summary of Registered Uses

Glufosinate ammonium is a water soluble herbicide applied as a foliar spray for the control of a broad spectrum of emerged grasses and broadleaf weeds. Glufosinate ammonium is the active ingredient in registered products used on transgenic field corn, soybeans and their associated raw agricultural commodities. Glufosinate ammonium is also the active ingredient in registered residential (outdoor, non-food) products for grass, brush and vine control around trees, shrubs, fences, walks, patios, driveways, sidewalks, on flower beds, and to non-selectively spot kill weeds in lawn. Section 18 emergency exemptions for use on sweet corn have been approved.

The registrant, AgrEvo USA Company, is requesting registration for use on transgenic canola, sugarbeets, and for desiccation on conventional potatoes. Application rates for the proposed uses range from 0.26 to 0.55 lb a.i. per acre. Both ground and aerial applications are permitted.

Table 1: Use Pattern and Formulation Information

Formulation Type, % ai	Equipment	Use Sites	Application rate range	Timing and frequency of applications	Comments
Liquid 18.19% ai	ground and aerial equipment	transgenic sugarbeets, canola	**sugarbeets:** 0.26 - 0.55 lb ai/acre; not to exceed 1.1 lbs ai/acre/growing season **canola:** 0.26 - 0.42 lb ai/acre; not to exceed 0.89 lbs ai/acre/growing season	**sugarbeets**: 3 X season; from the cotyledon stage up to 10 leaf stage; PHI= 60 days **canola:** 2 X season; from the cotyledon stage up to the early bolting stage repeat applications should be made when newly germinated weeds again reach 1 inch in height or diameter; PHI = 65 days	foliar active material with no soil-residual activity; rainfast 4 hrs. after application; to be applied to young, actively growing weeds
Liquid 11.3% ai		potatoes	0.38 lb ai/acre	apply at the beginning of natural senescence of potato vines; PHI= 9 days	

Occupational Exposure and Risk Assessment Characterization

The worker exposure and risk assessment presented in this document are based on the Pesticide Handler Exposure Database Version 1.1 (PHED, Surrogate Exposure Guide, August 1998) unit exposure estimates for workers wearing long pants, long sleeves, gloves (no gloves for aerial applicators), and using open cab ground equipment, and closed cab aerial equipment. There are no chemical specific data available to determine the potential risks associated with the proposed uses of glufosinate ammonium on transgenic canola, sugarbeets, and for desiccation of conventional potato vines.

Handler

Exposure Assumptions: The exposure assessment is based on the crop with the highest application rate (sugarbeets) and the crop with the highest average farm size (canola), as a conservative scenario. Commercial mixer/loaders (for aerial applications), commercial applicators (groundboom and aerial), and farmers (groundboom) treating their own fields were chosen as the most conservative scenarios. The occupational exposure assessment is based on the assumptions listed in Table 2.

Table 2: Assumptions for Worker Exposure Assessments

Exposure Scenario[1]	Unit Exposure ug/lb ai[2]		Application rate (lb ai/A)	Acres/Day[3]	Data source
	Dermal	Inhalation			
Mixer/Loader (aerial)	23	1.2	0.55	570	Unit exposures: Pesticide Handlers Exposure Database V1.1. Surrogate Exposure guide. August 1998. Estimates for all liquids, open mixing/loading: high confidence data Estimates for groundboom, open cab: medium confidence data Estimates for aerial/fixed-wing/closed cab/liquid: medium confidence data
Applicator (groundboom - open cab)	14	0.7	0.55	380	
Applicator (aerial - enclosed cockpits)	5	0.068	0.55	570	
Mixer/loader and applicator (groundboom)	37	1.9	0.55	190	Unit exposures were estimated by adding the M/L and applicator unit exposures

1 Handlers wearing long-sleeved shirt, long pants, and gloves (no gloves for aerial applicators)
2 Pesticide Handler Exposure Database Version 1.1 (PHED, Surrogate exposure Guide, August 1998)
3 Average canola farm is approximately 190 acres (United States 1997 Census of Agriculture, Table 42). Ground applicator assumed to treat 2 farms/day, aerial applicator assumed to treat 3 farms/day. The highest application rate and acreage from the proposed uses were used in this assessment.

Worker Exposure and Risk Assessment: Table 3 summarizes the worker exposure and risk estimates for commercial mixer/loaders, commercial applicators, and for farmers (m/l/a) treating their own fields. Short and intermediate-term exposures are expected for commercial applicators; only short-term exposures are expected for private applicators. Since workers are required to wear additional personal protective clothing (coveralls and protective eyewear) that are not accounted for in this assessment, the estimates of exposure are considered conservative.

Table 3: Occupational Exposure and Risk Estimates

Exposure Scenario	Unit Exposure (ug/lb ai)		Exposure[1] (mg/kg/day)			Short- & Intermediate - Term MOE[2]		
	Dermal	Inhalation	Dermal	Inhalation		Dermal	Inhalation	
				Short	Intermediate		Short	Intermediate
Mixer/ Loader	23	1.2	0.10	0.0054	0.0063	1000	1000	390
Applicator Groundboom - open cab	14	0.7	0.042	0.0021	0.0024	2400	3000	880
Applicator Aerial - enclosed cockpits	5	0.068	0.022	0.00031	0.00036	4600	20000	5800
Mixer/loader applicator (groundboom)	37	1.9	0.055	0.0028	0.0033	1800	2300	640

1 Exposure = Unit exposure × application rate × acres/day × 1/kg bw × .001mg/ug; 60 kg bw for short-term inhalation exposure, 70 kg bw for other exposures
2 Dermal NOAEL = 100mg/kg/day; Inhalation NOAEL = 6.3mg/kg/day and 2.1mg/kg/day for short-term exposure and intermediate- term exposures, respectively. MOE = NOAEL÷ Exposure; Level of concern = 100

The potential risks for occupational workers from short and intermediate-term exposures from the proposed uses of glufosinate ammonium on canola, sugarbeets, and potatoes do not exceed the Agency's level of concern. Chronic exposures are not expected from the proposed uses, therefore a risk assessment was not conducted.

Post-Application

There are no chemical-specific data available to determine the potential risks from post application activities associated with this proposed section 3 use of glufosinate ammonium. However, potential post-application exposures are not of concern, based on the use pattern, timing of applications, and the fact that planting and harvesting of the subject crops are mechanized. Most workers entering treated fields are likely to be performing low contact labor tasks such as mechanical incorporation and cultivation. Hoeing and scouting activities are also anticipated, but risks from these activities are not expected to exceed the Agency's levels of concern. For the purposes of the proposed use, reentry restrictions and personal protective clothing specified on the product label should provide adequate protection from the potential post-application exposures. Workers reentering treated fields before the required restricted entry interval are required to wear coveralls over short-sleeved shirts and short pants, chemical-resistant gloves, chemical resistant footwear and socks, and protective eyewear.

Restricted Entry Interval (REI): The interim restricted entry interval (REI) is 12 hours based on glufosinate ammonium's acute toxicity classification III for the dermal, inhalation, and ocular routes of exposure.

Residential Exposure

Glufosinate ammonium is registered for residential (outdoor, non-food) products as a non selective, postemergent herbicide. As such, it is primarily used as a spot treatment around trees, shrubs, fences, walks, patios, driveways, sidewalks, and flower beds. It is also registered for lawn renovation uses. There is no chemical specific data to assess exposures from the registered residential uses of glufosinate ammonium. The HED Exposure SAC considered these uses and recommended that the turf and garden scenarios, as specified in the Draft HED Standard Operating Procedures (SOPs) for Residential Exposure Assessments (18-DEC-1997), be used as a screening level assessment of the potential risks to homeowners from glufosinate ammonium use (see attachment, ***Minutes for Meeting of the Science Advisory Council for Exposure***).

Handler/Post-Application

The risk assessment was conducted using the following assumptions: dermal unit exposures of 100 mg/lb ai and 30 mg/lb ai, inhalation unit exposures of 30 ug/lb ai and 9.5 ug/lb ai for the garden and lawn renovation uses, respectively, maximum application rate of 1.4 lb ai/acre (product label), and a maximum area treated of 10,000 sq. ft. for the garden use scenario, 20,000 sq ft for the lawn renovation scenario, and 1,000 sq ft for "spot" lawn renovation scenario. Intermediate- and chronic-term residential exposures are not expected from the registered uses of glufosinate ammonium, therefore only short-term exposures were considered.

Table 4: Residential Handler Exposure and Risk Assessment

Scenario	Unit Exposure (mg/ lb ai)		Potential Dose Rate[1] (mg/kg/day)		Short -Term MOE[2]	
	Dermal	Inhalation	Dermal	Inhalation	Dermal	Inhalation
Garden use (low pressure hand wand)	100	0.030	0.46	1.4 E-4	*217*	45,000
Lawn renovation (full lawn; garden hose end sprayer)	30	0.0095	0.28	1.0 E-4	*360*	63,000
Lawn renovation (spot treatment; low pressure hand wand)	100	0.030	0.046	1.4 E-5	2200	450,000

1 Potential Dose Rate (PDR) = Unit exposure x Maximum application rate (1.4 lbs ai/acre) x Maximum area treated (garden use:10,000sq ft; lawn renovation: 20,000sq ft for full lawn and 1,000sq ft for spot treatment) ÷ kg bw (70 kg bw and 60 kg bw for short-term dermal and inhalation exposure, respectively. (Draft HED Standard Operating Procedures (SOPs) for Residential Exposure Assessments and Appendix B (18-DEC-1997)

2 Dermal NOAEL = 100 mg/kg/day; Inhalation NOAEL = 6.3 mg/kg/day for Short-term exposure; MOE = NOAEL/Exposure; Level of concern = 300

Table 5: Residential Post-Application Exposure and Risk Assessment [1]

Scenario	Transfer coefficient (cm^2/hr)	Potential Dose Rate[2] (mg/kg/day)	MOE[3]
Adult (garden use)	10,000	0.3	330
Children (garden use)	5,000	0.13	770
Adult (lawn renovation)	43,000	0.96	100
Children (lawn renovation)	8,700	0.91	110

1 Draft HED Standard Operating Procedures (SOPs) for Residential Exposure Assessments and Appendix B 18-DEC-1998). DFR_0 = Application rate x fraction available as residue (20% for garden use, 5% for lawn use: based on a decision of the Science Advisory Council for Exposure, see Minutes for Meeting of the Science Advisory Council for Exposure dated August 5, 1999) x 4.54E8 ug/lb x 2.47E-8 acre/cm^2 = 3.14 ug/cm^2 for garden use; 0.78 for lawn use

2 Potential post application dose rate= DFR x Transfer coefficient x Exposure time (garden use: 0.67 hr/ for adults, 0.33 hrs for children; lawn use: 2.0 hr) / BW (70 kg for adult, 39.1 for children (garden use) and 15 kg for children (lawn use) x 0.001mg/ug

3 Dermal NOAEL = 100 mg/kg/day; MOE = NOAEL/Exposure; Level of concern = 300

These estimates indicate that the potential risks from homeowner uses of glufosinate ammonium exceed the Agency's level of concern. The Agency's level of concern is for MOEs below 300. The dermal MOEs for homeowners applying glufosinate ammonium for the garden use is 217. The dermal MOEs for postapplication exposures from lawn renovation uses are 100 and 110 for adults and children, respectively. These estimates are based on screening level assumptions and therefore should be considered conservative.

In looking at these risk estimates it should be kept in mind that: **(1)** residential use of nonselective herbicides is likely to occur as a "spot spray" in small turf areas with a high content of non-desirable grasses or in areas that have been converted to some other uses such as vegetable or flower gardening. Lawn renovation treatment is recommended when 70% of the lawn is infested with undesirable lawn grasses (***Renovating your lawn, publication from Rutgers Cooperative Extension Service, N.J. Agricultural Experiment Station***). Therefore lawn renovation is considered a "last resort" treatment and a use pattern that is not likely to involve the average homeowner on a regular basis (scheduled treatments with selective herbicides to control undesirable weeds); **(2)** Information from Turfgrass Producers International (a not-for-profit trade association) indicates that "80% of nonselective herbicides production is used on new construction. with the remaining 20% going to golf courses, parks, sports fields, cemeteries, roadsides. etc. Exceptionally small amounts of turfgrass sod are used in lawn restoration projects"; **(3)** Information from AgrEvo indicates that sales of formulations containing glufosinate ammonium (Finale® Concentrate and Super Concentrate) sold to the homeowner lawn and garden market in 1998 represents a very small percentage of that for crops. It should also be considered that the SOP's assumptions for the garden scenario are based on a 10,000 sq ft "farm garden" which is not representative for the average homeowner. In addition, the lawn renovation scenario is based on transfer coefficients and assumptions used for regular lawn uses which are not necessarily applicable to lawn renovation uses and therefore, further overestimate the real potential risks.

Attachments:

Minutes for meeting of the Science Advisory Council for Exposure, July 22, 1999.

Renovating your lawn. publication from Rutgers Cooperative Extension Service, N. J. Agricultural Experiment Station.

AgrEvo USA Company. Reply to request for information on lawn renovation uses. Letter to J. Miller dated June 14, 1999.

cc: Chemical file (128850)
Myrta R. Christian, Olga Odiott (RAB 1/ HED)

Minutes

Meeting of the Science Advisory Council for Exposure
July 22, 1999 (1:30 to 3:00 p.m.: Room 810K)

Attendees: Jonathan Becker, Myrta Christian. Nader Tadayon, Shih-Chi Wang, Steve Weiss, Gary Bangs, Kelly O'Rourke, Julianna Cruz. Jack Arthur. Susan Hanley, Paula Deschamp, Joanne Miller, Eugene Wilson, Olga Odiott.

1. Triallate Open Cockpit Exposures – For triallate, the MOEs for aerial applicators in enclosed cockpits is acceptable, but PHED has insufficient data to estimate exposure from the aerial application of pesticides from open-cockpit airplanes. Exposure SAC Policy Number 6 addresses this issue, by stating *"If the estimated MOE for application of a given pesticide using closed-cockpit data from PHED or a pesticide-specific exposure study is an order of magnitude larger than the uncertainty factor (i.e., the acceptable MOE), then the use of an open-cockpit fixed-wing aircraft for application also should be acceptable."*

2. Copies of the results from the California School District Pesticide Survey were distributed. Any questions concerning this survey should be directed to Ruth Allen.

3. Availability of the "*Guidance for the Conduct of Residue Decline Studies for Use in Acute Dietary Probabilistic Risk Assessment*" was announced. Copies are available on OPP's web site or from David Miller.

4. The question concerning what clothing scenario is represented by the standard transfer coefficients values (Exposure SAC Policy Number 3) was again raised. These values represent workers dressed in long-sleeved shirt, long pants.

5. Pre-emergent herbicide issues raised by the registrant concerning pebulate were briefly discussed and several potential approaches were suggested to be explored during the development of HED's response.

6. Glufosinate ammonium – The Exposure SAC had a spirited discussion concerning the exposure assessment for glufosinate ammonium. Recommendations to the specific questions posed to the SAC are as follows:

Residential Handler Exposure Section

"... Therefore, the garden use could be considered the scenario with the highest potential for significant exposures. [Does the SAC agree with the last statement?]

Exposure SAC Response / Recommendation: No. Lawn renovation as described on the label would likely result in higher exposures.

[The SOP's assumption of 10.000 sq ft is based on a "farm garden" scenario and as such farm

equipment is likely to be used for such a large area. Does the SAC agree that 5,000 sq ft is a more realistic and still very conservative assumption of the average homeowner?]

Exposure SAC Response / Recommendation: No. Standard values in the residential SOPs (such as the area treated) should be used unless chemical- or use-specific information is available.

Questions to SAC

1) *Should we consider the garden use representative of a conservative residential exposure scenario for the registered used of glufosinate ammonium, and therefore the only one to be considered in the assessment?*

Exposure SAC Recommendation: No. Assessments should be conducted for the formulation being considered for the registration action and for all formulation types that would result in non-occupational (i.e., residential) exposure. Specifically for this chemical, additional homeowner and a PCO assessments should be done for lawn renovation use.

2) *Is it reasonable to assume that the estimated MOEs from lawn renovation uses represent overestimates of the real potential risks?*

Exposure SAC Recommendation: Not necessarily., It is suggested that the inputs to the assessment be characterized and that language concerning the "bounding" nature of the residential SOPs be added.

3) *Is it reasonable to use the transfer coefficients and assumptions for "regular" lawn uses for this specific scenario?*

Exposure SAC Recommendation: Yes. For postapplication assessments, the residential SOPs should be used. Standard values in the SOPs (such as the area treated) should be used unless chemical- or use-specific information is available.

4) *Do we meed to include a "whole lawn" renovation scenario in this assessment, and if so, which assumptions should we use?*

Exposure SAC Recommendation: Yes. Residential SOPs and labels should be used for the assessment.

5) *Do we need to aggregate the risks from both uses, or is it reasonable to assume that both scenarios (garden and lawn renovation) are not likely to occur simultaneously?*

Exposure SAC Recommendation: Details for aggregate assessments are still being developed. It is suggested that the risk for both scenarios be presented separately and characterized that it is unlikely (although possible) that the scenarios co-occur.

RUTGERS COOPERATIVE EXTENSION

NEW JERSEY AGRICULTURAL EXPERIMENT STATION

Renovating Your Lawn

James A. Murphy
Assistant Specialist in Turfgrass Management

Lawn areas which become unattractive and disappointing in performance generally contain a sparse and an unhealthy stand of lawn grasses. Also, an infestation of weeds is characteristic of these areas. Such conditions may result from one or more factors, such as: 1) Improper soil drainage, 2) Soil compaction, 3) Excessive shade, 4) Improper lawn grass for the location and/or use, 5) Soil pH - insufficient or excessive lime, 6) Improper fertilization - inadequate or excessive, 7) Chemical injury, 8) Mowing too closely, 9) Prolonged soil moisture stress - particularly in hot weather, 10) Improper watering techniques, 11) Excessive thatch accumulation, 12) Insect activity, 13) Disease damage, 14) Intensive use, and 15) Vandalism.

When the lawn area has adequate soil drainage and a relatively smooth contour and/or grade, renovation can correct unfavorable conditions, such as: 1) Sparse and uneven stand of desirable lawn grasses, 2) Infestation of undesirable broadleaf and grassy weeds, 3) Improper soil pH, 4) Low fertility, 5) Minor discrepancies in grade, 6) Soil surface compaction, 7) Excessive thatch accumulation, and 8) General neglect.

When considering improvement of a lawn area, specific renovation procedures are determined by:

1. Identifying the factor or factors which contributed to a failure of the lawn. If corrective steps are not taken, the net result may be an exercise in futility.
2. Evaluating the condition of the lawn in question to determine the most effective procedure.

Specific steps for renovating should be based on the condition of the lawn and problems needing attention. Four major categories of renovation are:

A. More than 30 percent desirable lawn grasses present.
B. Less than 30 percent desirable lawn grasses present and less than 1-inch of thatch.
C. Less than 30 percent desirable lawn grasses present and more than 1-inch of thatch.
D. Difficult to control undesirable perennial grasses infest the lawn.

Specific steps are outlined below.

A. **More than 30 percent** desirable lawn grasses are present:

1. Submit a representative sample of soil for determination of soil pH and nutrient status.
2. Apply an herbicide if necessary to control any broadleaf weeds, based upon the specific weed problem. 2,4-D alone is effective with dandelions, buckhorn and broadleaf plantains, and annual chickweed. For a wide variety of broadleaf weeds, combine herbicides for broad spectrum control, such as 2,4-D with Banvel*, MCPP, or 2,4-DP. Apply the selected herbicide at least 2 weeks before the seeding date and strictly follow the directions and precautions on the container.
3. Mow closely - set the mower at 3/4 to 1 inch.
4. Fill small isolated depressions in grade with high quality topsoil.
5. Apply lime based on a soil test.
6. Spread fertilizer based on a soil test. Nitrogen should be applied at 1 pound per 1000 square feet.
7. Dethatch (verti-groove) and/or core aerify with a machine specifically developed for this purpose. Adjust the rotating blades to penetrate completely through the thatch layer and at least 1/2 inch into the soil. Aerifying equipment should also penetrate through the thatch layer and 1 to 3 inches into the soil. Coring holes should have a maximum spacing of 3 inches.
8. Seed with a high-quality turfgrass mixture adapted to the intended use and expected level of

maintenance.

9. Drag the area with a steel door mat or a piece of cyclone fence when loose thatch material on the surface is relatively dry. Rake excessive thatch from the surface.
10. Water thoroughly. Light frequent watering (daily) may be continued to hasten germination and establishment of newly seeded lawn grasses.

Late summer to early fall is the most appropriate season for this procedure. Early spring is the next best choice. In the spring, however, success is usually more difficult. An increased weed problem, particularly crabgrass, can be expected from renovation in the spring. Applying siduron as a preemergence crabgrass herbicide, as the last step in the procedure, would be appropriate. More information on lawn establishment can be found in Rutgers Cooperative Extension publication FS 584, *Seeding Your Lawn.*

Various types of dethatching (verti-grooving) equipment are available. Only certain ones are effective and should be selected carefully for best results. The machine should have straight steel blades (at least 1/8 inch thick) spaced 1-1/2 to 2 inches apart, and be rigidly attached to the revolving shaft. Blade depth should be easily adjustable to allow complete penetration through the thatch layer and at least 1/2 inch into the soil. A small amount of soil will be displaced with a minimum disturbance of existing grade and desirable lawn grasses. Certain machines verti-groove and seed at the same time. The machine should provide conditions for seed-soil contact.

B. **Less than 30 percent** desirable lawn grasses are present with thatch layer less than 1 inch:

1. Test the soil - see procedure A.
2. Apply glyphosate according to directions and all precautions on the container. Glyphosate, a nonselective herbicide, will effectively eradicate plant growth in the treated area. It is available to homeowners under the product name: Kleen Up, and to professionals as: Roundup. Retreat areas which do not show complete eradication after 10 days.
3. Proceed as outlined in A, but <u>exclude</u> steps 1 and 2.

Generally, a lawn which has lost 70% or more of desirable grasses, becomes heavily infested with a variety of broadleaf and grassy weeds. In less common situations, where a serious weed problem has not infested the area, procedure "A" would be appropriate.

A lawn can be renovated with seeding or sodding. If immediate restoration is desired and/or the season is inappropriate for seeding, renovate with a high-quality sod. Follow the procedure outlined earlier and add this step: after complete eradication is achieved (Step 3), strip off the dead mat of grasses, weeds, and thatch.

A garden spade can be used to remove the dead mat, but a sod cutter (set to cut at the junction of thatch to soil) to remove this matted layer is most effective. After removal, proceed as outlined in "A," but <u>exclude</u> steps 1 and 2. Procedures for sodding are given in Rutgers Cooperative Extension publication FS 104, *Steps to an Instant Lawn.*

C. **Less than 30 percent** desirable lawn grasses are present with thatch layer of more than 1 inch:

Follow the procedure outlined for "B" and strip off the dead mat as outlined under "B." Whether seeding or sodding removing the thatch layer is essential for reestablishing desired lawn grasses.

D. **Difficult-to-control,** undesirable perennial grasses such as bentgrass, quackgrass, tall fescue, and orchardgrass infest the lawn area:

Follow procedure "B" or "C." Selective control of these undesirable perennial grasses in an otherwise satisfactory lawn is not available. To eliminate them, desirable lawn grasses must be sacrificed in a complete eradication procedure with glyphosate.

Renovation according to these four procedures for different lawn situations is an effective and efficient way of restoring lawn areas that have deteriorated. However, it will <u>not</u>, solve problems such as: soil drainage, deeply compacted soils, major deficiencies in grade, very rough surfaces, or phytotoxic soil contaminants. These conditions will require complete reconstruction procedures.

Other available references are: FS 102, *Your Lawn and Its Care.*

**Mention or display of a trademark, proprietary product, or firm in text or figures does not constitute an endorsement by Rutgers Cooperative Extension and does not imply approval to the exclusion of other suitable products or firms.*

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2M-9306-REV

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N.J. AGRICULTURAL EXPERIMENT STATION
RUTGERS, THE STATE UNIVERSITY OF NEW JERSEY
NEW BRUNSWICK

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AgrEvo®

VIA FAX: (703) 308-1825 & PAPER COPY BY MAIL

Ms. Joanne I. Miller
Product Manager (23)
Office of Pesticide Programs - H7504C
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, DC 20460-0001

June 14, 1999

Dear Ms. Miller:

Subject: Glufosinate-Ammonium Tolerance Petition
EPA Tolerance Petition 7F4910
Reply to Request for Information on Lawn Renovation Uses

I am writing in reply to your request for further information on the "lawn renovation" uses of glufosinate-ammonium herbicide products as shown on the labels for Finale® Super Concentrate Weed, Grass and Brush Killer (EPA Reg. No. 45639-191) and Finale® Concentrate Weed, Grass and Brush Killer (EPA Reg. No. 45639-193). In your voice mail to me on June 10, 1999 and our subsequent conversation on the same date, you have characterized the lawn renovation use directions as "pretty vague" and you have requested that we supply additional information regarding whether the whole lawn is treated (versus spot treatment), when the product is applied and how often it is used for this purpose. The information below details information pertinent to risk assessment for lawn renovation uses.

Label Directions for Lawn Renovation

A copy of the latest EPA-stamped approved label for Finale Super Concentrate is attached to this letter (Attachment 3).

The text of the labels for Finale Super Concentrate and Finale Concentrate are essentially identical and the use rates, on an active ingredient basis, are the same. The use directions for lawn renovation on the product labels are as follows:

> *"Apply Finale [Super] Concentrate to renovate lawns containing grassy and broadleaf weeds. Best results are obtained when at least one mowing is skipped prior to treatment. This allows the spray to contact more leaf surface area. Thorough coverage of all existing vegetation is necessary. Wait until the treated weeds are dead before reseeding or replanting the area to ensure that Finale [Super] Concentrate has had sufficient time to control the weeds. Best results are obtained on mixed grasses and weeds when 8 fluid ounces [4 fluid ounces for Super Concentrate] (16 tablespoons [8 tablespoons for Super Concentrate]) per gallon of water are used."*

AgrEvo USA Company
Little Falls Centre One, 2711 Centerville Road, Wilmington, DE 19808, Telephone: (302) 892-3000, Fax: (302) 892-3013

Re-entry Instructions

You said that Agency scientists have used very conservative assumptions to assess homeowner and/or home resident exposure to glufosinate-ammonium from lawn renovation uses. In the case of children, you said that it has been presumed that children may play on treated turf shortly after the product has been applied, even before the spray has dried, and that this results in unacceptably high exposures to glufosinate-ammonium.

Although we would like very much to examine the exposure and risk modeling results before we comment further on this matter, you have advised us that this is not possible at this time. Therefore, we must assume that the modelers have used overly conservative and perhaps too unrealistic presumptions in their calculations. To assume that children enter the treated area immediately after application, even before the spray has dried, is contradictory to specifically stated instructions in two sections of the use directions. These are:

[In the "Hazards to Humans and Domestic Animals" section]

"Do not allow children or pets to enter treated areas until the spray has dried."

[In the "Directions for Use" section]

"To avoid tracking product on to desirable vegetation, keep people and pets off treated areas until the spray is thoroughly dried."

If the preceding label precautions are observed, as required by law, we feel that the potential for product residue transfer to children and/or adults will undoubtedly be lower than the estimates that have likely been used by the Agency scientists in their first tier models.

Lawn Renovation Details: Frequency

Lawn renovation using Finale or other nonselective herbicides such as glyphosate is considered a "last resort" treatment used only when lawns have deteriorated to such an extent that salvage treatments are ineffective. When undesirable or unadapted grasses or broadleaf weeds dominate the turf, traditional selective weed control methods will not remediate the situation, and complete removal of the existing vegetation with a nonselective herbicide, followed by replanting or sodding is necessary. The Rutgers Cooperative Extension Service (Attachment 1) recommends complete eradication of the existing vegetation prior to reseeding only when the desirable lawn grasses are less than 30% of the total foliage.

Renovation with the use of nonselective herbicides is clearly, therefore, not an annual process and, in fact, is typically never required if the lawn is properly cared for. Relative to the total acreage of lawns in the US, the acreage requiring renovation in any given year is minor.

Lawn Renovation Details: Area

A component of the risk assessment for lawn renovation is the area that will be typically restored. Mr. Douglas Fender, Executive Director of the Turfgrass Producers International (a not-for-profit trade association) has advised AgrEvo in a letter dated June 11, 1999 (Attachment 2) that "nonselective herbicide treatments in residential settings would most likely occur on a 'spot spray' basis where small areas of turf are removed because of non-desirable grass infestations, or the lawn is being reduced for conversion to some other purpose such as for vegetable or flower gardening."

The label does not preclude the restoration of an entire lawn but the concept of assessing the treatment of "whole lawns" versus "partial lawns" is relative because of the very large variability of residential lot sizes. A "whole lawn" surrounding a smaller residence may be only be a fraction of the size of the lawn of a larger residential lot.

Consistent with Mr. Fender's statement, AgrEvo estimates that the average homeowner is unlikely to renovate more than 1,000 to 5,000 square feet of turf. This area assumption is based on the knowledge of the equipment generally available to homeowners, the time involved in preparing and cultivating new turf and the fact that large lawn owners are more likely to employ professional turf services. It should be noted, however, that our brands of glufosinate-ammonium products for professional use (Finale® Herbicide [EPA Reg. 45639-187] and Finale® VM Herbicide [EPA Reg. No. 45639-214]) and not labeled for lawn renovation uses.

A homeowner application of liquid nonselective herbicides would be made with either a pump-up pressure sprayer or a hose-end sprayer. The pump-up sprayers commonly sold in hardware and nursery/garden stores for home use are 1 to 3 gallon models that are not suitable for use to spray large areas greater than approximately 1,000 square feet. Hose-end sprayers with a coarse and short range spray pattern are also difficult and time consuming to use on surfaces greater than an approximate 5,000 square foot range.

Finale Homeowner Market Sales (Annual Poundage)

In earlier correspondence to you (letter from I. Kelly to J. Miller dated May 21, 1999), we provided confidential sales figures of Finale Super Concentrate and Finale Concentrate over the last five years. These figures show the most recent product sales in the year 1998 are equivalent to 51,000 (rounded to nearest 1,000) pounds of glufosinate-ammonium active ingredient. Historical sales (5 years) indicated that this was a steady to declining market. AgrEvo Environmental Health marketing and product development personnel have estimated that a only a very low percentage of this poundage is used in broadcast sprays on partial or complete lawns for the purpose of total vegetation control as part of lawn renovation. The bulk of the product use continues to be in spot or directed sprays for total weed control in cracks, crevices, trimming and edging in and around lawns and ornamental areas as opposed to on lawns by broadcast treatment.

Summary

In summary, the following points are pertinent to the risk assessment for the use of nonselective herbicides in lawn renovation:

- Nonselective herbicides are recommended in turf renovation only in cases of extreme deterioration when less than 30% of desirable lawn grasses are present
- Homeowners do not use nonselective herbicides in turf renovation on a frequent or regular basis
- Label directions prohibit re-entry into treated areas until sprays are dried.
- Homeowners are not expected to treat areas any larger than 1,000 to 5,000 square feet at any one time
- Total sales of Finale homeowner products are static to declining and represent a small percentage of the market with renovation serving a minor use within these sales

I hope that the preceding information provides the additional background material that you have requested and that you may proceed and complete your exposure and risk assessment analysis.

I will be traveling out of the country until June 21, 1999, however, Iain Kelly will be in the office and will be available for any additional information you may need. Iain will place a conference with me to you and Don Stubbs on Thursday, June 17, 1999 when Don returns to discuss the status of pending glufosinate-ammonium tolerance petition.

Very truly yours,

Victor A. Dorr

Victor A. Dorr
Manager, Regulatory Affairs
Phone: *(302) 892-3154*
Fax: *(302) 892-3099*
E-Mail: *victor.dorr@agrevo.com*

Attachment 1

FS108

RUTGERS COOPERATIVE EXTENSION

NEW JERSEY AGRICULTURAL EXPERIMENT STATION

Renovating Your Lawn

James A. Murphy
Assistant Specialist in Turfgrass Management

Lawn areas which become unattractive and disappointing in performance generally contain a sparse and an unhealthy stand of lawn grasses. Also, an infestation of weeds is characteristic of these areas. Such conditions may result from one or more factors, such as: 1) Improper soil drainage, 2) Soil compaction, 3) Excessive shade, 4) Improper lawn grass for the location and/or use, 5) Soil pH - insufficient or excessive lime, 6) Improper fertilization - inadequate or excessive, 7) Chemical injury, 8) Mowing too closely, 9) Prolonged soil moisture stress - particularly in hot weather, 10) Improper watering techniques, 11) Excessive thatch accumulation, 12) Insect activity, 13) Disease damage, 14) Intensive use, and 15) Vandalism.

When the lawn area has adequate soil drainage and a relatively smooth contour and/or grade, renovation can correct unfavorable conditions, such as: 1) Sparse and uneven stand of desirable lawn grasses, 2) Infestation of undesirable broadleaf and grassy weeds, 3) Improper soil pH, 4) Low fertility, 5) Minor discrepancies in grade, 6) Soil surface compaction, 7) Excessive thatch accumulation, and 8) General neglect.

When considering improvement of a lawn area, specific renovation procedures are determined by:

1. Identifying the factor or factors which contributed to a failure of the lawn. If corrective steps are not taken, the net result may be an exercise in futility.
2. Evaluating the condition of the lawn in question to determine the most effective procedure.

Specific steps for renovating should be based on the condition of the lawn and problems needing attention. Four major categories of renovation are:

A. More than 30 percent desirable lawn grasses present.
B. Less than 30 percent desirable lawn grasses present and less than 1-inch of thatch.
C. Less than 30 percent desirable lawn grasses present and more than 1-inch of thatch.
D. Difficult to control undesirable perennial grasses infest the lawn.

Specific steps are outlined below.

A. More than 30 percent desirable lawn grasses are present:

1. Submit a representative sample of soil for determination of soil pH and nutrient status.
2. Apply an herbicide if necessary to control any broadleaf weeds, based upon the specific weed problem. 2,4-D alone is effective with dandelions, buckhorn and broadleaf plantains, and annual chickweed. For a wide variety of broadleaf weeds, combine herbicides for broad spectrum control, such as 2,4-D with Banvel*, MCPP, or 2,4-DP. Apply the selected herbicide at least 2 weeks before the seeding date and strictly follow the directions and precautions on the container.
3. Mow closely - set the mower at 3/4 to 1 inch.
4. Fill small isolated depressions in grade with high quality topsoil.
5. Apply lime based on a soil test.
6. Spread fertilizer based on a soil test. Nitrogen should be applied at 1 pound per 1000 square feet.
7. Dethatch (verti-groove) and/or core aerify with a machine specifically developed for this purpose. Adjust the rotating blades to penetrate completely through the thatch layer and at least 1/2 inch into the soil. Aerifying equipment should also penetrate through the thatch layer and 1 to 3 inches into the soil. Coring holes should have a maximum spacing of 3 inches.
8. Seed with a high-quality turfgrass mixture adapted to the intended use and expected level of

maintenance.

9. Drag the area with a steel door mat or a piece of cyclone fence when loose thatch material on the surface is relatively dry. Rake excessive thatch from the surface.
10. Water thoroughly. Light frequent watering (daily) may be continued to hasten germination and establishment of newly seeded lawn grasses.

Late summer to early fall is the most appropriate season for this procedure. Early spring is the next best choice. In the spring, however, success is usually more difficult. An increased weed problem, particularly crabgrass, can be expected from renovation in the spring. Applying siduron as a preemergence crabgrass herbicide, as the last step in the procedure, would be appropriate. More information on lawn establishment can be found in Rutgers Cooperative Extension publication FS 584, *Seeding Your Lawn*.

Various types of dethatching (verti-grooving) equipment are available. Only certain ones are effective and should be selected carefully for best results. The machine should have straight steel blades (at least 1/8 inch thick) spaced 1-1/2 to 2 inches apart, and be rigidly attached to the revolving shaft. Blade depth should be easily adjustable to allow complete penetration through the thatch layer and at least 1/2 inch into the soil. A small amount of soil will be displaced with a minimum disturbance of existing grade and desirable lawn grasses. Certain machines verti-groove and seed at the same time. The machine should provide conditions for seed-soil contact.

B. **Less than 30 percent desirable lawn grasses are** present with thatch layer less than 1 inch:

1. Test the soil - see procedure A.
2. Apply glyphosate according to directions and all precautions on the container. Glyphosate, a nonselective herbicide, will effectively eradicate plant growth in the treated area. It is available to homeowners under the product name: Kleen Up, and to professionals as: Roundup. Retreat areas which do not show complete eradication after 10 days.
3. Proceed as outlined in A, but <u>exclude</u> steps 1 and 2.

Generally, a lawn which has lost 70% or more of desirable grasses, becomes heavily infested with a variety of broadleaf and grassy weeds. In less common situations, where a serious weed problem has not infested the area, procedure "A" would be appropriate.

A lawn can be renovated with seeding or sodding. If immediate restoration is desired and/or the season is inappropriate for seeding, renovate with a high-quality sod. Follow the procedure outlined earlier and add this step: after complete eradication is achieved (Step 3), strip off the dead mat of grasses, weeds, and thatch.

A garden spade can be used to remove the dead mat, but a sod cutter (set to cut at the junction of thatch to soil) to remove this matted layer is most effective. After removal, proceed as outlined in "A," but <u>exclude</u> steps 1 and 2. Procedures for sodding are given in Rutgers Cooperative Extension publication FS 104, *Steps to an Instant Lawn*.

C. **Less than 30 percent** desirable lawn grasses are present with thatch layer of more than 1 inch:

Follow the procedure outlined for "B" and strip off the dead mat as outlined under "B." Whether seeding or sodding removing the thatch layer is essential for reestablishing desired lawn grasses.

D. **Difficult-to-control**, undesirable perennial grasses such as bentgrass, quackgrass, tall fescue, and orchardgrass infest the lawn area:

Follow procedure "B" or "C." Selective control of these undesirable perennial grasses in an otherwise satisfactory lawn is not available. To eliminate them, desirable lawn grasses must be sacrificed in a complete eradication procedure with glyphosate.

Renovation according to these four procedures for different lawn situations is an effective and efficient way of restoring lawn areas that have deteriorated. However, it will <u>not</u> solve problems such as: soil drainage, deeply compacted soils, major deficiencies in grade, very rough surfaces, or phytotoxic soil contaminants. These conditions will require complete reconstruction procedures.

Other available references are: FS 102, *Your Lawn and Its Care*.

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TPI TURFGRASS PRODUCERS INTERNATIONAL

Attachment 2

June 11, 1999

RECEIVED
JUN 11 1999
V.A. DORR

Mr. Vic Dorr
AgrEvo USA Company

Dear Mr. Dorr:

We are pleased that you contacted this office seeking information about turfgrass and lawn renovation in the U.S.

Turfgrass Producers International is a 32-year-old, not-for-profit trade association, with more than 1,030 member companies in the U.S., Canada and 38 additional countries. Since 1993, TPI has supported the Turf Resource Center to assemble and distribute scientifically documented information related to all aspects of turfgrass to the public and other interested individuals or groups.

While exact figures are all but impossible to assemble, it is generally agreed that there are some 25,000,000 to 30,000,000 acres of maintained turfgrass in the U.S., with approximately 80% or over 20,000,000 acres in lawns (residential and commercial). Also, it is estimated that some 1,000,000 acres of turf are maintained as municipal, county and city parks. The 1997 *Census of Agriculture* (latest available) reports 302,930 acres devoted to turfgrass sod farms in the U.S.

From the Kline & Company chemical usage study of 1996 (the latest available), we know that glyphosate-based (or similar), non-selective herbicide products are the largest selling herbicide product to turfgrass sod farms. They estimate some 53.8 thousand gallons of this product type was used by turf farms. It is an essential component of turf production in order to assure high-quality, specie-pure turfgrass sod.

Residential use of this category of non-selective herbicide is very difficult to estimate. Based on the very small percentage of whole-lawn renovations that are known to take place, it could be reasonably concluded that only a fractional percentage of all home lawns are ever treated with this type product. It has been the turfgrass industry's experience that 80% of its production is used on new construction, with the remaining 20% going to golf courses, parks, sports fields, cemeteries, roadsides, etc. Exceptionally small amounts of turfgrass sod are used in lawn restoration projects.

Another conclusion that can reasonably be reached is that non-selective herbicide treatments in residential settings would most likely occur on a "spot-spray" basis where small areas of turf are removed because of non-desirable grass infestations, or the lawn area is being reduced for conversion to some other purpose such as for vegetable or flower gardening.

Sincerely,

Douglas H. Fender, Executive Director

Turfgrass Producers International · An International Organization Dedicated to Advancement of the Turfgrass Sod Industry
1855-A Hicks Road · Rolling Meadows, IL 60008 USA · 800/405-TURF (8873) · 847/705-9898 · FAX: 847/705-8347
Website: http://www.TurfgrassSod.org E-mail: Turf-Grass@msn.com

Attachment 3

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

RECEIVED
AUG - 4 1997
V.A. DORR

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

JUL 29 1997

Mr. Victor A. Dorr
AgrEvo USA Company
Little Falls Centre One
2711 Centerville Road
Wilmington, DE 19808

Dear Mr. Dorr:

Subject: Finale® Super Concentrate Weed and Grass Killer
EPA Registration No. 45639-191
Finale® Ready-to-Use Weed and Grass Killer
EPA Registration No. 45639-192
Finale® Concentrate Weed and Grass Killer
EPA Registration No. 45639-193
Your Letter Dated April 16, 1997, Response To Agency's Letter Dated June 1, 1995, Unacceptable Labeling Claims; and Your Resubmission Dated July 25, 1997

Your response to this Agency's letters of June 1, 1995 and April 25, 1997 have been reviewed. The proposed labeling for each of the subject pesticide products submitted with your letter dated July 25, 1997 is acceptable under the Federal Insecticide, Fungicide and Rodenticide Act, as amended, provided that you:

1. Make the optional claim "For Control of Weeds and Grasses for Home Use Only" not optional for the labeling of the subject products. Each of the labels must bear the claim "For Home Use Only" to remove these products from the EPA Worker Protection Standard requirements, as stated in PR Notice 93-7 and 93-11.

2. Delete the marketing claims:
   - o Not Harmful to Honey Bees.
   - o Not Harmful to Earthworms.
   - o Not Harmful to Honey Bees and Earthworms.

3. Submit one (1) copy each of the final printed labeling before you release the product for shipment under the revised labeling.

If these conditions are not complied with, the registrations will be subject to cancellation in accordance with FIFRA,

013728

section 6(e). Your release for shipment of the product(s) under the subject labeling constitutes acceptance of these conditions.

Stamped copies of the labels are enclosed for your records.

Sincerely yours,

Eugene M. Wilson
for Joanne I. Miller
Product Manager (23)
Herbicide Branch
Registration Division (7505C)

Enclosures (3)

Attachment 8: Rely® and Liberty™ labels

Edition #11: August 4, 1999

LIBERTY® HERBICIDE

A SELECTIVE HERBICIDE FOR USE ONLY ON SUGAR BEETS AND CANOLA RESISTANT TO THE ACTIVE INGREDIENT IN THIS PRODUCT. AGREVO USA COMPANY RECOMMENDS USE ONLY ON SEED DESIGNATED AS LIBERTYLINK® OR WARRANTED BY AGREVO USA COMPANY AS BEING RESISTANT TO LIBERTY HERBICIDE

ACTIVE INGREDIENT:	
Glufosinate-ammonium† (CAS Number 77182-82-2)	18.19%*
OTHER INGREDIENTS	81.81%
TOTAL	100.00%

*Equivalent to 1.67 pounds of active ingredient per U.S. gallon.

† Protected by U.S. Patent No 4,400,196

KEEP OUT OF REACH OF CHILDREN

WARNING - AVISO

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

EPA Registration Number 45639-199

EPA Establishment Numbers: 45639-MI-001
407-IA-2

Net Contents: 1 Gallon, 2.5 Gallons, 15 Gallons, 60 Gallons, 120 Gallons & Bulk

See side/back panel for First Aid statements

AgrEvo®

AgrEvo USA Company
Little Falls Centre One
2711 Centerville Road
Wilmington, DE 19808

FIRST AID

If Swallowed: Rinse mouth thoroughly with plenty of water. Do **NOT** induce vomiting. Get medical attention immediately.

If in Eyes: Flush with plenty of water. Get medical attention if irritation persists.

If on Skin: Remove contaminated clothing. Wash skin immediately with plenty of soap and water. Get medical attention.

If Inhaled: Remove individual to fresh air. Get medical attention if breathing difficulty develops.

NOTE TO PHYSICIAN

If this product is ingested, endotracheal intubation and gastric lavage should be performed as soon as possible, followed by charcoal and sodium sulfate administration. **Additionally, call 1-800-471-0660 immediately for further information.**

IN CASE OF MEDICAL, ENVIRONMENTAL, OR TRANSPORTATION EMERGENCIES OR INQUIRIES, CALL 1-800-471-0660 (24 HOURS/DAY).

For product inquiry information, call toll free: 1-877-GO LIBERTY [1-877-465-4237] or visit the LibertyLink worldwide web site at www.liberty-link.com

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS AND DOMESTIC ANIMALS
WARNING

May be fatal if absorbed through skin. Causes moderate eye irritation. Harmful if swallowed. Do not get in eyes, on skin, or on clothing. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash clothing before reuse.

Personal Protective Equipment (PPE)
Some materials that are chemical-resistant to this product are listed below. If you want more options, follow the instructions for category C on an EPA chemical resistance category selection chart.

Applicators and other handlers must wear:
Coveralls worn over short-sleeved shirt and short pants; chemical-resistant gloves such as barrier laminate, butyl rubber ≥14 mils, nitrile rubber ≥14 mils, neoprene rubber ≥14 mils, polyvinyl chloride (PVC) ≥14 mils, or Viton® ≥14 mils; chemical resistant footwear plus socks; protective eyewear. Wear a chemical resistant apron when mixing/loading and cleaning equipment.

Discard clothing and other absorbent materials that have been drenched or heavily contaminated with this product's concentrate. Do not reuse them. Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

Engineering control statement:
When handlers use closed systems, enclosed cabs, or aircraft in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides [(40 CFR 170.240(d)(4-6)], the handler PPE requirements may be reduced or modified as specified in the WPS.

USER SAFETY RECOMMENDATIONS

Users should:

- Wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet.
- Remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.
- Remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing.

ENVIRONMENTAL HAZARDS

Do not apply directly to water, to areas where surface water is present, or to intertidal areas below the mean high water mark. Do not contaminate water by cleaning of equipment or disposal of equipment washwaters.

STORAGE AND DISPOSAL

Do not contaminate water, food, or feed by storage or disposal.

Do not use or store near heat or open flame. Keep the container tightly closed and dry in a cool, well-ventilated place. Storage temperature should be between 32°F and 85°F, with a maximum of 125°F. Protect against direct sunlight.

PESTICIDE DISPOSAL: Wastes resulting from the use of this product may be disposed of on-site or at an approved waste disposal facility.

CONTAINER DISPOSAL: *[1 and 2½ Gallon Containers Only]*
Empty containers should be triple rinsed (or equivalent), then offer for recycling or reconditioning; or puncture and dispose of in a sanitary landfill, or by incineration; or, if allowed by State and local authorities, by burning. If burned, stay out of smoke.

[15 Gallons, 60 Gallons, 120 Gallons & Bulk Containers Only]
This is a sealed returnable container to be used only for Liberty Herbicide. When this container is empty, it must not be opened, cleaned, or discarded. Empty containers must be returned to the original purchase location.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. Do not use this product until you have read the entire label. Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application.

For any requirements specific to your State or Tribe, consult the agency responsible for pesticide regulation.

AGRICULTURAL USE REQUIREMENTS

Use this product only in accordance with its labeling and with the Worker Protection Standard, 40 CFR part 170. This Standard contains requirements for the protection of agricultural workers on farms, forests, nurseries, and greenhouses, and handlers of agricultural pesticides. It contains requirements for training, decontamination, notification, and emergency assistance. It also contains specific instructions and exceptions pertaining to the statements on this label about personal protective equipment (PPE), and restricted-entry intervals. The requirements in this box only apply to uses of this product that are covered by the Worker Protection Standard.

Do not enter or allow worker entry into treated areas during the restricted entry-interval (REI) of 12 hours.

PPE required for early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil, or water, is: coveralls worn over short-sleeved shirt and short pants; chemical-resistant gloves such as barrier laminate, butyl rubber ≥14 mils, nitrile rubber ≥14 mils, neoprene rubber ≥14 mils, polyvinyl chloride (PVC) ≥14 mils or Viton ≥14 mils; chemical resistant footwear plus socks; protective eyewear.

GENERAL INFORMATION

Liberty Herbicide is a water-soluble herbicide for application as a foliar spray for the control of a broad spectrum of emerged grass and broadleaf weeds in sugar beets and canola. This product is for use only on sugar beets and canola resistant to the active ingredient in this product. AgrEvo USA Company recommends use only on sugar beets and canola designated as LibertyLink® or warranted by AgrEvo USA Company as being resistant to Liberty Herbicide. The basis of selectivity of Liberty Herbicide in sugar beets and canola is the presence of a gene in LibertyLink or other sugar beet and canola varieties warranted by AgrEvo which allows the plant to detoxify the active ingredient of Liberty Herbicide.

IMPORTANT CROP SAFETY INFORMATION
READ BEFORE USING THIS PRODUCT

Liberty Herbicide is for use only on sugar beets and canola resistant to the active ingredient in this product. AgrEvo USA Company recommends use only on sugar beets and canola designated as LibertyLink or warranted by AgrEvo USA Company as being resistant to Liberty Herbicide.

The basis of selectivity of Liberty Herbicide in sugar beets and canola is the presence of a gene in LibertyLink or other sugar beet and canola varieties warranted by AgrEvo which allows the plant to detoxify the active ingredient of Liberty Herbicide.

Use of Liberty Herbicide on sugar beets or canola not designated as LibertyLink or not warranted by AgrEvo may result in severe crop injury and/or yield loss.

Do not allow spray to contact foliage or green tissue of desirable vegetation other than sugar beets and canola resistant to the active ingredient in this product. This product may injure or kill all green vegetation contacted by the spray other than LibertyLink or other sugar beet and canola varieties warranted by AgrEvo.

AgrEvo does not warrant the crop safety or weed control of this product if used on sugar beet or canola varieties other than those designated as LibertyLink or warranted by AgrEvo to safely withstand the application of Liberty Herbicide.

APPLICATIONS DIRECTIONS FOR USE ON SUGAR BEETS

THOROUGH SPRAY COVERAGE IS VERY IMPORTANT. Liberty Herbicide works best when weeds are actively growing.

APPLICATION TIMING

Applications of Liberty Herbicide on sugar beets may be made from the cotyledon stage up to the 10 leaf stage of the sugar beet. Liberty Herbicide is a foliar-active material with no soil-residual activity. For best results, apply to emerged, young actively growing weeds. Weeds that emerge after application will not be controlled. Liberty Herbicide will have an effect on weeds that are larger than the recommended leaf stage, however speed of activity and control may be reduced. Weed control may be reduced when heavy dew is present or when weeds are under stress due to drought, cool temperatures or extended periods of cloudiness. Liberty Herbicide is rainfast four (4) hours after application, and rainfall within four (4) hours may necessitate retreatment.

For best weed control and sugar beet yield, Liberty Herbicide applications should begin when weeds are up to 1 inch in height or diameter. Repeat applications should be made when newly germinated weeds again reach 1 inch in height or diameter. Liberty Herbicide will control weeds larger than 1 inch in height or diameter, however higher use rates and multiple applications will be required. Do not apply more than 84 ounces of this product per growing season.

Liberty Herbicide should be applied at the rate recommended in the *Rate Recommendation Tables for Weed Control* in the *Application Methods* section of this label.

RESTRICTIONS TO THE DIRECTIONS FOR USE

1. Application is recommended for use only on sugar beets designated as LibertyLink or warranted by AgrEvo USA Company to safely withstand the application of Liberty Herbicide. Application to sugar beet varieties not designated LibertyLink or otherwise authorized by AgrEvo may result in severe crop injury and/or yield loss.

2. Avoid drift to desirable vegetation.

3. A cultivation may be made at least 5 days before or after a Liberty Herbicide application.

4. Clean sprayer thoroughly before mixing Liberty Herbicide, particularly if a herbicide with the potential to injure crops was previously used.

5. Thoroughly triple rinse sprayer and use a commercial tank cleaner before using in crops not designated as LibertyLink or warranted by AgrEvo USA Company to safely withstand the application of Liberty Herbicide. Make sure any rinsate or foam is thoroughly removed from spray tank and boom. Rinsate may be disposed of in non-crop areas that do not contain desirable vegetation.

6. **DO NOT** apply more than 42 ounces per acre of Liberty Herbicide in one application and **DO NOT** apply more than 84 ounces per acre of Liberty Herbicide on the sugar beet crop per growing season.

7. **DO NOT** apply Liberty Herbicide within 60 days of harvesting sugar beets

8. **DO NOT** plant rotation crops in a field treated with Liberty Herbicide for 120 days after the last application of this product with the exception of wheat, barley, buckwheat, millet, oats, rye, sorghum, and triticale which may be planted 70 days after the last application of this product. Corn and soybeans may be planted at any time.

9. **DO NOT** graze the treated crop or cut for hay.

10. **DO NOT** add surfactants. Anti-foams, drift control agents or a spray grade or a liquid formulation of ammonium sulfate may be added if needed.

11. **DO NOT** apply Liberty Herbicide if sugar beets show injury from prior herbicide applications or environmental stress (drought, excessive rainfall, etc.).

12. **DO NOT** apply this product through any type of irrigation system.

MIXING INSTRUCTIONS

Liberty Herbicide must be applied with properly calibrated and clean equipment.

Liberty Herbicide is specially formulated to mix readily in water. Prior to adding Liberty Herbicide to the spray tank, ensure that the spray tank is thoroughly clean (see *Cleaning Instructions*).

1. Fill tank to one-half full with clean water prior to adding Liberty Herbicide.

2. Add the correct amount of Liberty Herbicide.

3. Add the remaining amount of water, begin agitation, and spray out immediately.

4. The addition of an anti-foaming agent may reduce foaming, especially when using soft water.

NOTE: Ensure that all circuits (pipes, booms, etc.) have the correct concentration of Liberty Herbicide/water mixture before the application is started. Keep bypass line on or near bottom of tank to minimize foaming.

CLEANING INSTRUCTIONS

Before and after using Liberty Herbicide, always complete a thorough cleaning of the spray tank, lines and filter. Spray equipment should be thoroughly rinsed using a strong detergent solution.

APPLICATION METHODS

Do not use flood jet nozzles, controlled droplet application equipment or air-assisted spray equipment. Uniform, thorough spray coverage is important to achieve consistent weed control.

For ground application: Refer to the *Rate Recommendation Tables for Weed Control* for proper application rates. DO NOT apply when winds are gusty, or when conditions will favor movement of spray particles off the desired spray target. To avoid drift and insure consistent weed control, apply Liberty Herbicide with the spray boom as low as possible while maintaining a uniform spray pattern. Liberty Herbicide should be applied broadcast in a minimum of 10 gallons of water per acre using a minimum spray pressure of 40 pounds per square inch and a maximum ground speed of 10 mph. The use of 80 degree or 110 degree flat fan nozzles is highly recommended for optimum spray coverage and canopy penetration. Application of the spray at a 45 degree angle forward will result in better spray coverage. **Under dense weed/crop canopies, a broadcast rate of 15-20 gallons of water per acre should be used so that thorough spray coverage will be obtained.**

For aerial application: Calibrate the spray equipment prior to use. Liberty Herbicide should be applied in a minimum of 5 gallons of water per broadcast acre. To get uniform spray coverage, use nozzles to provide 200-350 micron size droplets. DO NOT use raindrop nozzles. Aerial applications with this product should be made at a maximum height of 10 feet above the crop with low drift nozzles at a maximum pressure of 40 psi. Avoid application under conditions where uniform coverage cannot be obtained or where excessive spray drift may occur.

RATE RECOMMENDATION TABLES FOR WEED CONTROL

Liberty Herbicide rates in ounces (pints) of formulated product per acre for the control of weeds at maximum growth stages are shown in the following tables. In weed populations with mixed species, apply the rate needed for all species present.

Grass Weeds	Maximum Growth Stage of Weed* (Leaves/Height/)		Comments on Weed Growth Stage/ Application Timing/ Number of Applications
	20 fl.oz./A (1.25 pt./A)	28 fl.oz./A (1.75 pt./A)	
Barley, volunteer	2 leaf (2")	3 leaf (3")	Multiple applications may be required
Barnyardgrass	3 leaf (2")	5 leaf (3")	Maximum of 1 tiller
Corn, volunteer	2 leaf (3")	4 leaf (6")	---
Crabgrass, large	3 leaf (2")	5 leaf (3")	Maximum of 1 tiller
Crabgrass, smooth	3 leaf (2")	5 leaf (3")	Maximum of 1 tiller
Cupgrass, woolly	5 leaf (4")	(8")	---
Foxtail, giant	4 leaf (3")	6 leaf (4")	Maximum of 2 tillers
Foxtail, green	4 leaf (3")	6 leaf (4")	Maximum of 2 tillers
Foxtail, yellow	3 leaf (1")	4 leaf (2")	Apply prior to tillering
Millet, volunteer proso	3 leaf (2")	5 leaf (3")	Maximum of 1 tiller
Millet, wild proso	3 leaf (2")	5 leaf (3")	Maximum of 1 tiller
Oat, wild	2 leaf (2")	3 leaf (3")	Maximum of 1 tiller
Panicum, fall	3 leaf (2")	5 leaf (3")	Maximum of 1 tiller
Panicum, Texas	3 leaf (2")	5 leaf (3")	Maximum of 1 tiller
Sandbur, field	---	4 leaf (2")	Apply prior to tillering
Wheat, volunteer	2 leaf (2")	3 leaf (3")	Maximum of 1 tiller

* Apply up to 42 fluid ounces/acre (2.63 pints/acre) if weeds exceed the growth stage shown in the table.

For improved control of heavy populations or larger than recommended volunteer wheat, volunteer barley, yellow foxtail, and wild oats, Liberty Herbicide can be tank mixed with Assure® II Herbicide, Poast® Herbicide, Prism® Herbicide or Select® 2EC Herbicide.

Perennial Weeds	Maximum Growth Stage of Weed* (Height/Diameter)		Comments on Number of Applications
	20 fl.oz./A (1.25 pt./A)	28 fl.oz./A (1.75 pt./A)	
Quackgrass	---	3 leaf (3")	Multiple applications required
Sowthistle, perennial	---	4 leaf (3")	Multiple applications required
Thistle, Canada	---	4 leaf (3")	Multiple applications required

* Apply up to 42 fluid ounces/acre (2.63 pints/acre) if weeds exceed the growth stage shown in the table.

Broadleaf Weeds	Maximum Growth Stage of Weed* (Leaves/Diameter)	
	20 fl.oz./A (1.25 pt./A)	28 fl.oz./A (1.75 pt./A)
Buckwheat, wild	4 leaf (2")	6 leaf (3")
Buffalobur	4 leaf (2")	6 leaf (3")
Carpetweed	---	4 leaf (2")
Chickweed, common	4 leaf (2")	6 leaf (3")
Cocklebur, common	6 leaf (3")	8 leaf (5")
Kochia	(1")	(2")
Ladysthumb	2 leaf (1")	4 leaf (3")
Lambsquarter, common	2 leaf (1")	5 leaf (3")
Mallow, Venice	4 leaf (2")	6 leaf (3")
Marshelder	2 leaf (1")	4 leaf (2")
Mustard, wild	4 leaf (2")	6 leaf (3")
Nightshade, eastern black	4 leaf (2")	6 leaf (3")
Pigweed, prostrate	(1")	(3")
Pigweed, redroot	2 leaf (1")	4 leaf (3")
Pigweed, smooth	2 leaf (1")	4 leaf (3")
Pigweed, spiny	2 leaf (1")	4 leaf (3")
Purslane, common	(1")	(2")
Ragweed, common	6 leaf (3")	8 leaf (5")
Ragweed, giant	4 leaf (2")	6 leaf (3")
Sheperd's purse	4 leaf (2")	6 leaf (3")
Smartweed, Pennsylvania	2 leaf (1")	4 leaf (3")
Sowthistle, annual	4 leaf (2")	6 leaf (3")
Sunflower, common	6 leaf (3")	8 leaf (5")
Thistle, Russian	(1")	(2")
Velvetleaf	2 leaf (1")	4 leaf (3")

* Apply up to 42 fluid ounces/acre (2.63 pints/acre) if weeds exceed the growth stage shown in the table.

APPLICATIONS DIRECTIONS FOR USE ON CANOLA

THOROUGH SPRAY COVERAGE IS VERY IMPORTANT. Liberty Herbicide works best when weeds are small and are actively growing. In situations when weed populations are high, early removal of weeds is important to prevent stressing the canola due to weed competition.

APPLICATION TIMING

Applications of Liberty Herbicide on canola may be made from the cotyledon stage up to the early bolting stage of the canola. Slight discoloration of the canola may be visible after application. This effect is temporary and will not influence crop growth, maturity or yield. Liberty Herbicide is a foliar-active material with no soil-residual activity. For best results, apply to emerged, young actively growing weeds. Weeds that emerge after application will not be controlled. Liberty Herbicide will have an effect on weeds that are larger than the recommended leaf stage, however speed of activity and control may be reduced. Weed control may be reduced when heavy dew is present or when weeds are under stress due to drought, cool temperatures or extended periods of cloudiness. Liberty Herbicide is rainfast four (4) hours after application, and rainfall within four (4) hours may necessitate retreatment.

RESTRICTIONS TO THE DIRECTIONS FOR USE

1. Application is recommended for use only on canola designated as LibertyLink or warranted by AgrEvo USA Company to safely withstand the application of Liberty Herbicide. Application to canola varieties not designated LibertyLink or otherwise authorized by AgrEvo may result in severe crop injury and/or yield loss.

2. Avoid drift to desirable vegetation.

3. Clean sprayer thoroughly before mixing Liberty Herbicide, particularly if a herbicide with the potential to injure crops was previously used.

4. Thoroughly triple rinse sprayer and use a commercial tank cleaner before using in crops not designated as LibertyLink or warranted by AgrEvo USA Company to safely withstand the application of Liberty Herbicide. Make sure any rinsate or foam is thoroughly removed from spray tank and boom. Rinsate may be disposed of in non-crop areas that do not contain desirable vegetation.

5. **DO NOT** use on canola in the states of Alabama, Delaware, Georgia, Kentucky, Maryland, New Jersey, North Carolina, South Carolina, Tennessee, Virginia and West Virginia

6. **DO NOT** apply more than 68 ounces per acre of Liberty Herbicide for weed control on the canola crop per growing season or more than 120 ounces per acre of Liberty Herbicide for segregate control during seed production per growing season.

7. **DO NOT** apply Liberty Herbicide within 65 days of harvesting canola.

8. **DO NOT** plant rotation crops in a field treated with Liberty Herbicide for 120 days after the last application of this product with the exception of wheat, barley, buckwheat, millet, oats, rye, sorghum, and triticale which may be planted 70 days after the last application of this product. Corn and soybeans may be planted at any time.

9. **DO NOT** graze the treated crop or cut for hay.

10. **DO NOT** add surfactants. Anti-foams or drift control agents may be added if needed.

11. **DO NOT** apply Liberty Herbicide if canola shows injury from prior herbicide applications or environmental stress (drought, excessive rainfall, etc.).

12. **DO NOT** apply this product through any type of irrigation system.

13. **DO NOT** tank mix Liberty Herbicide with other pesticides including herbicides unless recommended on this label.

14. AgrEvo USA Company does not warrant the safety or performance of this product when used on "brown bag" or farmer-saved seed (bin run seed).

Spray Additives

Liberty Herbicide must be applied with ammonium sulfate (AMS). Use only fine-feed grade or spray grade AMS at 3 pounds per acre. Do not add any surfactants or crop oils. Antifoams or drift control agents may be added if needed.

MIXING INSTRUCTIONS

Liberty Herbicide must be applied with properly calibrated and clean equipment.

Liberty Herbicide is specially formulated to mix readily in water. Prior to adding Liberty Herbicide to the spray tank, ensure that the spray tank is thoroughly clean (see *Cleaning Instructions*).

1. Fill tank to one-half full with clean water.

2. Add the appropriate amount of AMS to the spray tank.

3. If tank mixing with a graminicide, add the correct amount of the graminicide.

4. Add the correct amount of Liberty Herbicide.

5. Add the remaining amount of water, begin agitation, and spray out immediately.

The addition of an antifoaming agent may reduce foaming, especially wnen using soft water.

NOTE: Ensure that all circuits (pipes, booms, etc.) have the correct concentration of Liberty Herbicide/water mixture before the application is started. Keep bypass line on or near bottom of tank to minimize foaming.

CLEANING INSTRUCTIONS

Before and after using Liberty Herbicide, always complete a thorough cleaning of the spray tank, lines and filter. Spray equipment should be thoroughly rinsed using a strong detergent solution.

APPLICATION METHODS

Do not use flood jet nozzles, controlled droplet application equipment or air-assisted spray equipment. Uniform, thorough spray coverage is important to achieve consistent weed control.

For ground application: Refer to the *Rate Recommendation Tables for Weed Control* for proper application rates. DO NOT apply when winds are gusty, or when conditions will favor movement of spray particles off the desired spray target. To avoid drift and insure consistent weed control, apply Liberty Herbicide with the spray boom as low as possible while maintaining a uniform spray pattern. Liberty Herbicide should be applied broadcast in a minimum of 10 gallons of water per acre using a minimum spray pressure of 40 pounds per square inch and a maximum ground speed of 10 mph. The use of 80 degree or 110 degree flat fan nozzles is highly recommended for optimum spray coverage and canopy penetration. Application of the spray at a 45 degree angle forward will result in better spray coverage. **Under dense weed/crop canopies, a broadcast rate of 15-20 gallons of water per acre should be used so that thorough spray coverage will be obtained.**

For aerial application: Calibrate the spray equipment prior to use. Liberty Herbicide should be applied in a minimum of 5 gallons of water per broadcast acre. To get uniform spray coverage, use nozzles to provide 200-350 micron size droplets. DO NOT use raindrop nozzles. Aerial applications with this product should be made at a maximum height of 10 feet above the crop with low drift nozzles at a maximum pressure of 40 psi. Avoid application under conditions where uniform coverage cannot be obtained or where excessive spray drift may occur.

RATE RECOMMENDATION TABLES FOR WEED CONTROL

Rates in ounces (pints) of formulated product per acre for the control of weeds at selected heights are shown in the following tables. In weed populations with mixed species, apply the rates needed for all species present.

Liberty Herbicide at 34 fl. oz./A (2.1 pt./A) plus Ammonium Sulfate

Grass Weeds	Growth Stage of Weed (Leaves/Max. Height)	Comments
Barley, volunteer*	1-3 leaves (3")	A second application may be required
Foxtail, yellow	1-4 leaves (2")	Apply prior to tillering
Sandbur, field		
Oat, wild	1-4 leaves (4")	Maximum of 1 tiller; a second application may be required
Wheat, volunteer		
Corn, volunteer	1-4 leaves (6")	---
Barnyardgrass	1-5 leaves (3")	Maximum of 1 tiller
Crabgrass, large		
Crabgrass, smooth		
Millet, volunteer proso		
Millet, wild proso		
Panicum, fall		
Panicum, Texas		
Foxtail, giant	1-6 leaves (4")	Maximum of 2 tillers
Foxtail, green		
Cupgrass, woolly	1-8"	---

* Suppression only

For improved control of heavy populations or larger than recommended volunteer wheat, volunteer barley, yellow foxtail, and wild oats, Liberty Herbicide can be tank mixed with Assure® II Herbicide at 0.3 pt./A, or Poast® Herbicide at 0.4 pt./A.

Liberty Herbicide at 34 fl. oz./A (2.1 pt./A) plus Ammonium Sulfate

Perennial Weeds	Growth Stage of Weed (Leaves/Max. Height)	Comments
Quackgrass	1-4 leaves (4")	Top growth control; a second application may be required.
Sowthistle, perennial	1-6 leaves (4")	
Thistle, Canada		

Liberty Herbicide at 34 fl. oz./A (2.1 pt./A) plus Ammonium Sulfate

Broadleaf Weeds	Growth Stage of Weed (Leaves/Max. Height)	Comments
Buckwheat, wild	1-3 leaves	Up to 1" in height
Pigweed, redroot		Up to 2" in height
Carpetweed	1-4 leaves	Up to 2" in height
Lambsquarter, common		
Marshelder		
Ladysthumb		Up to 3" in height
Pigweed, smooth		
Pigweed, spiny		
Smartweed, Pennsylvania		
Velvetleaf		
Mustard, wild	1-5 leaves	Up to 3" in height
Buffalobur	1-6 leaves	Up to 3" in height
Chickweed, common		
Mallow, Venice		
Nightshade, eastern black		
Ragweed, giant		
Shepherd's purse		
Sowthistle, annual		
Cocklebur, common	1-8 leaves	Up to 5" in height
Ragweed, common		
Sunflower, common		
Kochia	1-2"	---
Thistle, Russian		---
Pigweed, prostrate	1-3"	---
Purslane, common		---
Waterhemp, tall		---
Wormwood, biennial		---
Pennycress, field	1-4"	---
Dandelion	1-6"	Diameter of rosette

Rate Recommendation for Use in Canola Seed Propagation

For the detection and control of susceptible canola "segregates" during canola seed production only, Liberty Herbicide may be applied at up to 40 fluid ounces (2.5 pints) per acre on canola from the cotyledon stage up to the early bolting stage of the canola. Applications may be repeated, if necessary, up to three times in one growing season.

Do not apply more than 120 ounces of product per acre to canola being grown for seed production in one growing season.

IMPORTANT: READ BEFORE USE

By using this product, user or buyer accepts the following conditions, warranty, disclaimer of warranties and limitations of liability.

AgrEvo USA Company does not warrant the safety or performance of this product when used on "brown bag" or farmer-saved seed (bin run seed).

CONDITIONS: The directions for use of this product are believed to be adequate and should be followed carefully. However, because of extreme weather conditions and soil conditions, manner of use and other factors beyond AgrEvo USA Company's control, it is impossible for AgrEvo USA Company to eliminate all risks associated with the use of this product. As a result, crop injury or ineffectiveness is always possible. All such risks shall be assumed by the user or buyer.
DISCLAIMER OF WARRANTIES: THERE ARE NO WARRANTIES, EXPRESS OR IMPLIED, OF MERCHANTABILITY OR OF FITNESS FOR A PARTICULAR PURPOSE OR OTHERWISE, WHICH EXTEND BEYOND THE STATEMENTS MADE ON THIS LABEL. No agent of AgrEvo USA Company is authorized to make any warranties beyond those contained herein or to modify the warranties contained herein. AgrEvo USA Company disclaims any liability whatsoever for incidental or consequential damages, including, but not limited to, liability arising out of breach of contract, express or implied warranty (including warranties of merchantability and fitness for a particular purpose), tort, negligence, strict liability or otherwise.
LIMITATIONS OF LIABILITY: THE EXCLUSIVE REMEDY OF THE USER OR BUYER FOR ANY AND ALL LOSSES, INJURIES OR DAMAGES RESULTING FROM THE USE OR HANDLING OF THIS PRODUCT, WHETHER IN CONTRACT, WARRANTY, TORT, NEGLIGENCE, STRICT LIABILITY OR OTHERWISE, SHALL NOT EXCEED THE PURCHASE PRICE PAID, OR AT AGREVO USA COMPANY'S ELECTION, THE REPLACEMENT OF PRODUCT.

Trademark Information:

Assure II is a trademark of DuPont Company
Viton is a trademark of DuPont Dow Elastomers
Poast is a trademark of BASF Corporation
Prism and Select are trademarks of Valent U.S.A. Corporation
Liberty® and LibertyLink® are registered trademarks of Hoechst Schering AgrEvo GmbH

Edition #3: August 4, 1999

RELY® HERBICIDE

FOR POTATO VINE DESICCATION

ACTIVE INGREDIENT:
Glufosinate-ammonium† (CAS Number 77182-82-2) 11.33%*

OTHER INGREDIENTS 88.67%
TOTAL 100.00%

*Equivalent to 1.00 pound of active ingredient per U.S. gallon.

† Protected by U.S. Patent No 4,400,196

KEEP OUT OF REACH OF CHILDREN

WARNING – AVISO

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

EPA Registration Number 45639-187 EPA Establishment Numbers: 45639-MI-001
407-IA-2

Net Contents: [Various Sizes]

See side/back panel for First Aid statements

AgrEvo®

AgrEvo USA Company

Little Falls Centre One
2711 Centerville Road
Wilmington, DE 19808

FIRST AID

If Swallowed: Rinse mouth thoroughly with plenty of water. Do **NOT** induce vomiting. Get medical attention immediately.

If in Eyes: Flush with plenty of water. Get medical attention if irritation persists.

If on Skin: Remove contaminated clothing. Wash skin immediately with plenty of soap and water. Get medical attention.

If Inhaled: Remove individual to fresh air. Get medical attention if breathing difficulty develops.

NOTE TO PHYSICIAN

If this product is ingested, endotracheal intubation and gastric lavage should be performed as soon as possible, followed by charcoal and sodium sulfate administration. **Additionally, call 1-800-471-0660 immediately for further information.**

IN CASE OF MEDICAL, ENVIRONMENTAL, OR TRANSPORTATION EMERGENCIES OR INQUIRIES, CALL 1-800-471-0660 (24 HOURS/DAY).

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS AND DOMESTIC ANIMALS
WARNING

Causes substantial but temporary eye injury. Harmful if swallowed, inhaled or absorbed through skin. Avoid contact with skin, eyes or clothing. Avoid breathing vapor or spray mist.

Personal Protective Equipment

Some materials that are chemical-resistant to this product are listed below. If you want more options, follow the instructions for category C on an EPA chemical resistance category selection chart.

Applicators and other handlers must wear:

Long-sleeved shirt and long pants; chemical-resistant gloves such as barrier laminate, butyl rubber ≥14 mils, nitrile rubber ≥14 mils, neoprene rubber ≥14 mils, polyvinyl chloride (PVC) ≥14 mils or Viton® ≥14 mils; shoes plus socks; protective eyewear.

Discard clothing and other absorbent materials that have been drenched or heavily contaminated with this product's concentrate. Do not reuse them. Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

USER SAFETY RECOMMENDATIONS

Users should:

- Wash hands before eating, drinking, chewing gum, using tobacco or using the toilet.
- Remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.
- Remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing.

ENVIRONMENTAL HAZARDS

Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Do not clean equipment or dispose of equipment washwaters in a manner that will contaminate water resources or arable land. Glufosinate-ammonium and its degradates have those properties normally associated with pesticides that have been detected in groundwater. Use of this product in areas with coarse soils and high water tables may result in groundwater contamination.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.
Do not use or store near heat or open flame.

PESTICIDE DISPOSAL: Wastes resulting from the use of this product may be disposed of on site or at an approved waste disposal facility.

CONTAINER DISPOSAL: Empty containers should be triple rinsed (or equivalent). Then offer for recycling or reconditioning, or puncture and dispose of in a sanitary landfill, or by incineration, or, if allowed by State and local authorities, by burning. If burned, stay out of smoke.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. Do not use this product until you have read the entire label.
Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application.

For any requirements specific to your State or Tribe, consult the agency responsible for pesticide regulation.

AGRICULTURAL USE REQUIREMENTS

Use this product only in accordance with its labeling and with the Worker Protection Standard, 40 CFR part 170. This Standard contains requirements for the protection of agricultural workers on farms, forests, nurseries, and greenhouses, and handlers of agricultural pesticides. It contains requirements for training, decontamination, notification, and emergency assistance. It also contains specific instructions and exceptions pertaining to the statements on this label about personal protective equipment (PPE), and restricted-entry intervals. The requirements in this box only apply to uses of this product that are covered by the Worker Protection Standard.

Do not enter or allow worker entry into treated areas during the restricted entry-interval (REI) of 12 hours.

PPE required for early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil, or water, is: coveralls; chemical-resistant gloves such as barrier laminate, butyl rubber >14 mils, nitrile rubber >14 mils, neoprene rubber >14 mils, polyvinyl chloride (PVC) >14 mils or viton >14 mils; shoes plus socks; protective eyewear.

GENERAL INFORMATION

Rely® Herbicide is a nonselective herbicide for application as a foliar spray for use in potato vine desiccation. THOROUGH SPRAY COVERAGE IS IMPORTANT. Visual effects from application of Rely Herbicide occur within 2 to 4 days after application under good growing conditions.

Avoid all contact with foliage or green tissue of desirable vegetation. This product may injure or kill growing plants that receive spray drift or if they receive spray mixture containing Rely Herbicide by error or accident. If desirable vegetation is contacted, rinse the sprayed portion with water immediately to reduce potential injury.

POTATO VINE DESICCATION

Apply Rely Herbicide at a rate of 3 pints per acre in 20 to 100 gallons water per acre with ground equipment or in 5 to10 gallons per acre with aerial equipment. Use sufficient water for thorough coverage of potato vines. Where crop canopy is dense, better spray coverage will be achieved with the higher spray volumes.

For best results apply Rely Herbicide at the beginning of natural senescence of potato vines. Do not harvest potatoes earlier than 9 days after application. Do not apply to potatoes grown for seed stock.

Do not plant rotation crops in a field treated with Rely Herbicide for 120 days after the last application of this product with the exception of wheat, barley, buckwheat, millet, oats, rye, sorghum, and triticale which may be planted 70 days after the last application of this product. Corn and soybeans may be planted at any time.

IMPORTANT: READ BEFORE USE

By using this product, user or buyer accepts the following conditions, warranty, disclaimer of warranties and limitations of liability.

CONDITIONS: The directions for use of this product are believed to be adequate and should be followed carefully. However, because of extreme weather conditions and soil conditions, manner of use and other factors beyond AgrEvo USA Company's control, it is impossible for AgrEvo USA Company to eliminate all risks associated with the use of this product. As a result, crop injury or ineffectiveness is always possible. All such risks shall be assumed by the user or buyer.

DISCLAIMER OF WARRANTIES: THERE ARE NO WARRANTIES, EXPRESS OR IMPLIED, OF MERCHANTABILITY OR OF FITNESS FOR A PARTICULAR PURPOSE OR OTHERWISE, WHICH EXTEND BEYOND THE STATEMENTS MADE ON THIS LABEL. No agent of AgrEvo USA Company is authorized to make any warranties beyond those contained herein or to modify the warranties contained herein. AgrEvo USA Company disclaims any liability whatsoever for incidental or consequential damages, including, but not limited to, liability arising out of breach of contract, express or implied warranty (including warranties of merchantability and fitness for a particular purpose), tort, negligence, strict liability or otherwise.

LIMITATIONS OF LIABILITY: THE EXCLUSIVE REMEDY OF THE USER OR BUYER FOR ANY AND ALL LOSSES, INJURIES OR DAMAGES RESULTING FROM THE USE OR HANDLING OF THIS PRODUCT, WHETHER IN CONTRACT, WARRANTY, TORT, NEGLIGENCE, STRICT LIABILITY OR OTHERWISE, SHALL NOT EXCEED THE PURCHASE PRICE PAID, OR AT AGREVO USA COMPANY'S ELECTION, THE REPLACEMENT OF PRODUCT.

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